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A. E. FAVORSKII (1860-1945) (ON THE HUNDREDTH ANNIVERSARY OF HIS BIRTH)

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Leningrad State University

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During the sixty-five years of his scientific activity, Aleksei Evgrafovich Favorskii made a great contribution to the development of organic chemistry and entered into its history as one of the outstanding classic investigators. As the founder and head of one of the largest scientific schools, the responsible editor of a principal chemical journal, and a prominent representative of the national chemical community, A. E. was, over the course of many years, an authoritative leader and organizer of our chemical science and chemical industry, and the tutor of several generations of chemists.

The role of A. E. as scientist, teacher, and worker for our society obliges us to make a thorough and penetrating study of his life and his creativity, and the image of A. E. as man, citizen, and scientist should be a living and graphic example by which we can train the new generations of our scientific staffs.

A. E's. world outlook was formulated and completed under the conceptual influence of the Russian revolutionary democrats and progressive, democratically attuned Russian scientists. A. E., without doubt, absorbed deeply and forever the materialistic world viewpoint, and took up the best and highest ideas of democracy, the renowned traditions, high culture, and deep patriotism of the great Russian scientists.

Coming forward with a word of reply at the solemn assembly in honor of his 80th birthday in the Moscow House of Learning, he said: ". . . for my success in this work I am fortunately indebted to the combination of circumstances under which I was obliged to start my scientific research. I was fortunate enough to enter St. Petersburg University as a student, where such leaders as D. I. Mendeleev, A. M. Butlerov, N. A. Menshutkin, and D. P. Konovalov represented chemical science, and there I again was fortunate enough to enter the laboratory of A. M. Butlerov, the 'head of the school of Russian chemists,' as he is usually called."

There is no doubt that A. E. showed himself to be possessed of an outstanding, original, and brilliant national talent as a scientist. He was certainly a highly gifted man with a lively interest in the most diverse manifestations of life; he reacted actively toward the historical and political events that were taking place, and he deeply understood and felt the spirit of the times. He was far from the type of cloistered investigator, and invariably lived a full and active scientific and social life. Therefore it is no accident that after the Great October Socialist Revolution he immediately appeared among the best and most advanced of the Soviet professorships. In all his social-organizational, scientific, and pedagogical activity during many years he carried on a very determined and active battle with stagnation, conservatism, and outmoded traditions. It should be emphasized that precisely his clear and deep understanding of his duty as a citizen to his fatherland and his government underlaid and determined the success of his many-sided activities. He always considered that his private and personal interests were incidental and transitory and this principle comprised the firm basis of his whole life.

As a scientist and teacher A. E. also built all of his activity toward the protection of the interests of genuine science, and in this his consistency and principles were beyond reproach. He recognized only a forward and

progressive movement in the development of science. Being very conscious not only of the value and the fruitfulness, but also of the weakness of his own hypotheses and theories, A. E. maintained and defended them only while they made it possible to visualize and set up a broadly conceived experiment, and he always kept in mind that they were subject to unavoidable further development. With all his deserved authority and erudition and his love of science, A. E. was invariably simple and modest. This established his strength as a scientist, and this attracted to him students of all ages. All knew very well that he was extremely demanding, but they also knew that he could help them and teach them "how science is made."

A. E. founded the largest scientific school in organic chemistry, numbering more than two hundred chemical research workers, among them: the late S. V. Lebedev, K. A. Krasusskii, A. E. Porai-Koshits, V. N. Ipat'ev, B. V. Byzov, V. N. Krestinskii, Zh. I. Iotsich, K. I. Debu, Yu. S. Zal'kind, I. N. Nazarov, E. V. Alekseevskii, M. M. Kucherov, V. M. Tolstopyatov, V. S. Batalin, et al., and also among those now working fruitfully: S. N Danilov, É. D. Venus-Danilova, A. A. Vansheidt, A. F. Dobryanskii, N. A. Domnin, I. A. D'yakonov, T. A. Favorskaya, T. I. Temnikova, T. E. Zalesskaya, A. I. Zakharova, M. F. Shostakovskii, A. I. Lebedeva, A. M. Khaletskii, V. I. Nikitin, I. A. Shikhiev, V. I. Egorova, F. Ya. Perveev, I. A. Favorskaya, K. A. Ogloblin, et.al.

All of A. E's studies represent a single logical investigative process of development of his basic ideas and views. In connection with this, Academician N. Ya. Dem'yanov writes: "Most of A. E's investigations flow logically one from the other" [1].

A. E. clearly understood the tremendous significance of organic synthesis, the goal of which almost never is attained by chance. Evaluating the significance of A. E's. contributions in the field of the development of organic synthesis in general and the synthesis of acetylenic hydrocarbons and their derivatives in particular, A.N . Nesmeyanov and M.I. Kabachnik write: "The original and powerful trend in Soviet synthetic organic chemistry associated with the acetylenic hydrocarbons and the diene hydrocarbons, which are of so much practical importance, had its origin with A. E. Favorskii and his pupil S. V. Lebedeva. Favorskii laid down the principles of our knowledge of the acetylenic hydrocarbons, their conversions to diene hydrocarbons, and their various functional derivatives, and these principles were broadly developed by him and his students and extended far beyond the limits of the chemistry of the acetylenes."

All of A. E's. research investigations were so rich in their inherent content, that even at the present time they constitute a golden fund for organic chemistry and chemical industry.

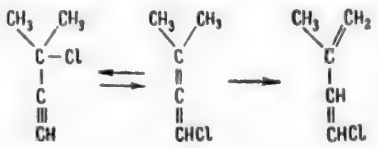
The great and fruitful scientific activity of A. E. began in the 80's of the last century and became most successful and valuable in the Soviet period, when the Great October Socialist Revolution created all the conditions for the manifestation of his talent as a scientific theorist and brilliant experimenter.

As we already have said, the scientific activity of A. E. Favorskii began in the laboratory of the founder and creater of the theory of the structure of organic compounds, A. M. Butlerov [2]. By then the statistical aspect of this theory had been completed and proved in its last essentials, and he was concentrating his attention on the study of molecular dynamics in the broad sense of the term.

A. E. immediately entered into this field of organic chemistry. By a complicated and difficult route, but comparatively quickly, A. E. arrived at the discovery of isomeric conversions in the series of acetylenic, allenic, and dienic hydrocarbons. Later, on the basis of his numerous investigations, the well-known Favorskii rules for the isomerization of unsaturated hydrocarbons were discovered.

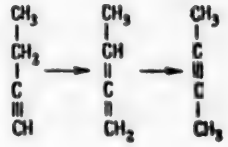
Considerably later, the investigations in this field were extended to various functional derivatives of the unsaturated hydrocarbons, and A. E. considered the isomeric conversions as typical allylic rearrangements [3].

The broad range of experimental material available at the present time permits consideration of these rearrangements as prototropic isomeric conversions [4]. To this field belongs the acetylene–allene–1,3-diene rearrangement, discovered and thoroughly investigated by T. A. Favorskaya [5].

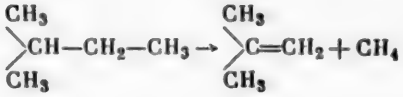


It proceeds in the first stage as an anionotropic rearrangement, and in the second stage as a prototropic allylic rearrangement [4].

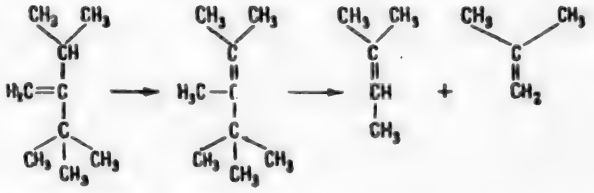
The conversion of monosubstituted acetylenes to disubstituted derivatives, which was studied by A. E., also can be considered as a double prototropic rearrangement.



A. E. compared these rearrangements with those conversions in which rupture of simple carbon–carbon bonds had been observed [3].

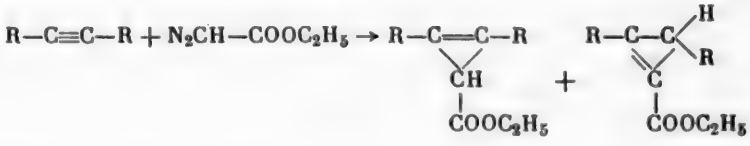


I. N. Nazarov [6] had observed this type of breakdown in the catalytic isomerization of isopropyl-tert-butylethylene.



As can be seen, the facts established by A. E. and the hypotheses that he advanced for their explanation served in the perfection and deepening of the theories of organic chemistry. A very strong connection can be seen between the theoretical viewpoints of A. E., on the one hand, and the contemporary electronic representations, on the other.

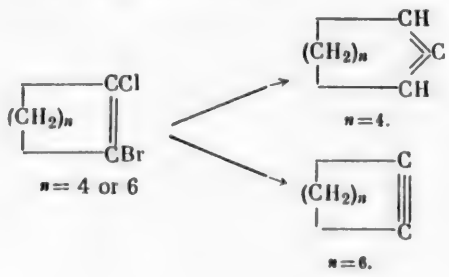
In connection with the discovery of the rules in the field of the stability and the conversions of unsaturated hydrocarbons of the aliphatic series, A. E. was profoundly interested in the same problems also in relation to the cyclic hydrocarbons. The first of these to be considered were the small rings with 3 and 4 members, then the usual rings with 5 to 7 members, intermediate ones with 8 to 12 members, and those with 12 and more [7]. The problem of whether cyclopropene, methylenetrimethylene, and their derivatives could exist, was investigated by A. E. and I. A. D'yakonov. At the present time the latter [8], employing the reaction of diazoacetic ester with the acetylenic hydrocarbons, has obtained homologs of the ester of cyclopropenecarboxylic acid [9].



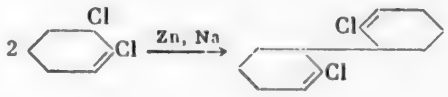
The derivatives of cyclopropene have a complex of intrinsic, interesting properties, which determine the ability of these compounds to form stable cations and anions of an aromatic character.

Over a long period A. E. had a lively interest also in the 4- to 8-membered polymethylene rings. In particular he was especially interested in the question of whether these rings could exist with triple or allene bonds in the cycle. In collaboration with V. N. Bozhovskii [10], N. A. Domnin [11], V. I. Nikitin [12], and M. F. Shostakovskii [13], he carried out a series of systematic investigations for the purpose of studying the stability and the isomeric conversions of polymethylene rings with multiple bonds.

The most interesting and significant results in this field were the preparation of a seven-membered ring with an allene bond and an eight-membered ring with an acetylenic bond [11].



It was shown that when zinc and sodium act on 1,2-dichlorocyclohexene-1, a six-membered ring with an allene bond is not formed, but the reaction goes in the direction of the coupling of two molecules of the starting unsaturated dichloride,



as a result of which bis(2,2-dichlorobicyclohexenyl-1,1') is formed [11].

The reaction with 1,2-dichlorocyclopentene-1 goes in the same way.

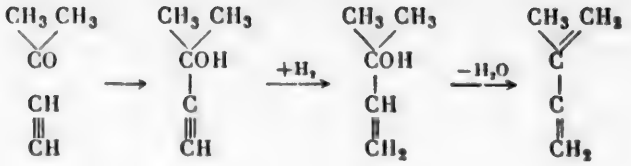
It was established that when the diene dibromide 2,3-dibromocyclohexadiene-1,3 reacts with metallic sodium, the splitting out of two atoms of bromine proceeds to completion only in the direction of the formation of the polymeric product $(C_6H_6)_n$, and that the benzene expected from this reaction is not formed [11].

The investigation of the course of this reaction is of considerable interest.

As a result of the work that was carried out, A. E. arrived at important generalizations: 1) In four-membered rings acetylenic, allenic, and dienic systems are impossible, since the strain produced in their formation would be too great; 2) in five- and six-membered rings neither acetylenic nor allenic bonds are possible, but these rings can exist with 1,3- and 1,4-diene bonds; 3) in a seven-membered ring an acetylenic bond is impossible, but an allenic one is possible; 4) in larger rings an acetylenic bond also is possible [14]. All of these conclusions were fully confirmed experimentally by A. E. himself and his students.

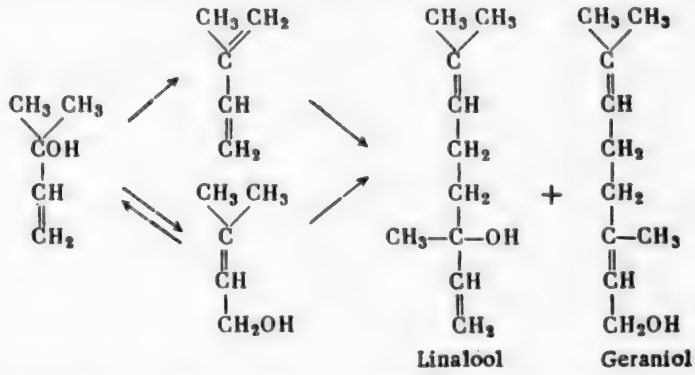
In carrying out the synthesis of unsaturated rings by A. E. Favorskii's method, it has been established that HCl splits out from the mixed α-chlorodibromides of five- and six-membered rings, but HBr splits out from the seven- and eight-membered ones, as happens also in the aliphatic series. A. E. gave an original stereochemical explanation for these facts [15].

The different mobility of the hydrogen atoms in C-H bonds especially interested A. E. during all of his scientific activity. The mobility of hydrogen, which appears distinctly in the presence of alkaline catalysts, is responsible, in A. E's. opinion, for the ability of the molecules to undergo isomeric conversions and condensations. Proceeding from these observations, A. E. arrived at the idea of the possibility of the condensation in the presence of caustic alkali of monosubstituted acetylenic hydrocarbons with ketones because of the mobile acetylenic hydrogen. The first attempt at condensation of phenylacetylene with acetone was successful [16]. This type of condensation was carried out by A. E. and his co-workers for acetylene itself, as a result of which they obtained an acetylenic alcohol, which also proved to be a starting material for various conversions. This condensation reaction has great theoretical and practical significance and is now widely used in laboratory practice. On the basis of this A. E. and A. I. Lebedova [17] developed a method for the preparation of isoprene.



It is known that isoprene is the basic structural unit of natural rubber, and thus is it possible to prepare isoprene rubber by A. E's. method.

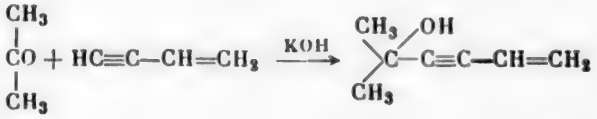
After the preparation of linalool and geraniol by A. I. Lebedeva, starting with dimethylvinylcarbinol and γ,γ-dimethylallyl alcohol A. E. proposed a scheme for the production of terpene alcohols.



Linalool Geraniol

A. E. assumed that alcohols of the composition $C_5H_{10}O$ are formed in nature from leucine.

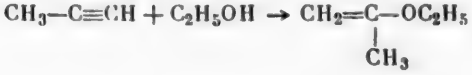
Applying the Favorskii condensation reaction to vinyllacetylene, I. N. Nazarov [18] obtained vinylethyldimethylcarbinol.



Later on I. N. Nazarov and co-workers, starting with this and similar alcohols, carried out a large number of varied syntheses of polymerized unsaturated compounds, some of which proved to be of practical value. Vinylethyldimethylcarbinol itself, because of its ability to polymerize, was used by Nazarov for the preparation of a technically valuable gum carbinol.

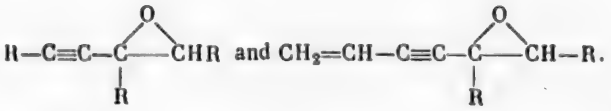
The numerous investigations by Nazarov made possible the appearance of a whole series of compounds having technically valuable properties of one sort or another. Thus promedol and isopromedol were made [19] and found use as effective anodynes.

In 1886 A. E. had observed that methylacetylene upon being heated with alcoholic potassium hydroxide added ethyl alcohol at the triple bond to form an unsaturated ether [20].

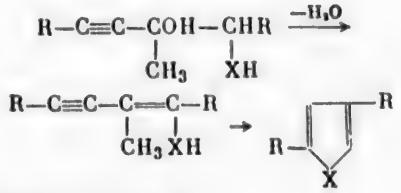


A. E. also showed that the unsaturated ether obtained was comparatively easily decomposed in 1% aqueous sulfuric acid solution to acetone and ethyl alcohol. This reaction for the synthesis of the inyl ethers from alcohols and acetylene proved to be very fruitful [21] and was carried out by M. F. Shostakovskii on a manufacturing scale. M. F. Shostakovskii [22] and his co-workers investigated the vinyl ethers in detail and on a broad scale and showed that they are capable of yielding valuable polymers and copolymers. They also provided a basis for numerous syntheses of medicines, solvents, etc.

A. E. and his students in 1940 carried out interesting investigations on the synthesis and isomerization of oxides of the acetylene and vinylacetylene series [37]. In recent years F. Ya. Perveev [38] has developed the synthesis of oxides of the type



The addition of ammonia, hydrogen sulfide, or hydrogen selenide to these oxides leads to the formation of derivatives of pyrrole, thiophene, or selenophene.



where X = O, N, S, Se.

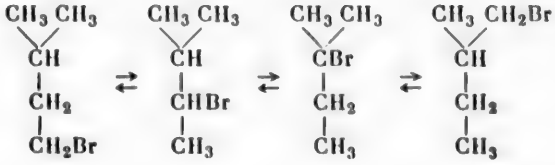
Thus, F. Ya. Perveev developed a new one-stage method for the synthesis of very valuable heterocyclic compounds.

It would not be too much to say that the fundamental problem in all the theoretical investigations and experimental studies of A. E. is the problem of isomeric conversions and molecular rearrangements. Investigating the conversion of the acetylenic and allenic hydrocarbons, A. E. together with K. I. Debu [23] showed that the isomeric conversions are reversible. Thus, it was shown that isopropylacetylene and dimethylallene form equilibrium mixtures, which are obtained under the action of alcoholic alkali and metallic sodium. Monosubstituted acetylenic hydrocarbons isomerize through the allenic ones to disubstituted acetylenes. Diacetylenic hydrocarbons with isolated triple bonds isomerize to acetylenes with conjugated bonds.

$$HC{\equiv}C{-}CH_2{-}CH_2{-}C{\equiv}CH \rightarrow CH_3{-}C{\equiv}C{-}C{\equiv}C{-}CH_3$$

A. E. considered that the cause that gave rise to the direction of this polymerization was the striving of the isomeric forms to accumulate methyl groups in the molecule and concentrate multiple bonds, providing conditions for the great stability of these forms [24]. This is confirmed by present thermodynamic data.

In A. E's. opinion, isomeric conversions make it possible to discover the internal dynamics of the molecules and their state at the time of movement, and to establish which of the isomeric forms will be thermodynamically more stable, and which less so. This also determined his interest in isomeric conversions and molecular rearrangements. In this connection the investigation by A. E. and his co-workers [25] of the reversible conversions of isomeric bromides having the same hydrocarbon skeleton is of great theoretical interest. When one of the bromides was heated at 210°, a mixture was obtained,



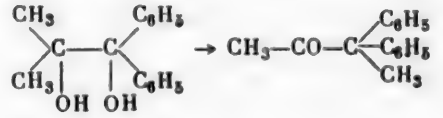
The tertiary isomer predominated in quantity, followed by the secondary isomer, with the primary isomer occupying last place. In this work A. E. combined reversible isomeric conversions and the phenomenon of tautomerism in one general group under the general term "phenomena of equilibrium isomerism." He considered that the difference between tautomeric and reversible isomeric conversions is only quantitative in nature [26].

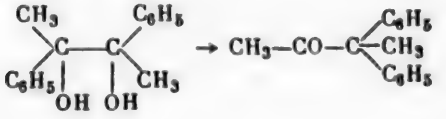
These ideas of A. E. offer great prospective developments even at the present time, since the scope of the phenomena relating to them may be very broad, and precise chemical, physicochemical, and physical methods for the determination of the composition of mixtures have reached a considerable degree of perfection.

Having established on the basis of the experimental material of his doctoral dissertation the hypothesis of the isomeric conversions of chlorinated alcohols, ketones, aldehydes, carbinols, and hydroxycarbinols, A. E. set up all of his subsequent investigations in these fields of organic chemistry with a certain and clear goal. They were undertaken both to verify the proposed hypothesis and for the purpose of confirming particular conclusions and consequences resulting from the hypothesis itself, or, finally, they pursued the goal of resolving contradictions arising in the science. This hypothesis in the hands of A. E. proved to be extraordinarily fruitful, and he developed it with invariable success during the course of his whole life. As a result, with the aid of his hypothesis, A. E. not only achieved a relatively simple generalization of a large field of phenomena, but at the same time correctly foretold a whole series of new reactions.

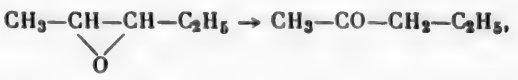
In the light of this hypothesis, A. E. gave a penetrating explanation of such complex and interesting phenomena as alcoholic fermentation, the Cannizaro reaction, benzil conversion, the contraction of polymethylene rings, the reduction of nitro compounds to amines, of thiosulfates to sulfites and hydrogen sulfide, and of diethyl sulfide to ethyl mercaptan, etc.

In the 70's and 80's of the last century important chemists began to pay particular attention to molecular rearrangements, and especially to pinacoline rearrangements, trying to find rules controlling these conversions. The cause of these rearrangements was said to be the different affinity of the radicals (Meervein) or the different migrational ability of the radicals (Tiffeno). In contrast to these and other investigators, A. E. considered it impossible to explain the direction of these conversions merely by the properties of the radicals. He expressed the idea that the stability of the end product under the reaction conditions is the principal cause directing the process in one direction or another. Thus, A. E. considered the dehydration of α-glycols as a reaction of simultaneous oxidation and reduction; the direction of this reaction depends on the greater capacity of one of the two hydroxylated carbons to be oxidized. This also would be the principal cause directing the process of conversion, and the shifting of the radicals would only be a result of this cause. Consequently, the striving to form a stable acetyl group directs the process in just that direction, when one of the radicals is a methyl group.

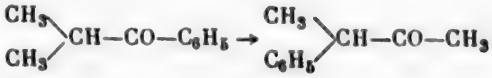




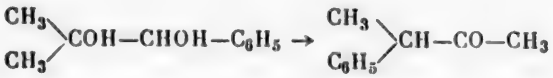
In confirmation of this conclusion, A. E. and M. N. Chechenkin [27] carried out the isomeric conversion of methylethylethylene oxide to methyl propyl ketone



while according to Meervein's affinity theory diethyl ketone should have been formed in this reaction. A. E. considered that the ketone that was most stable under the conditions of the reaction would also be the one formed as a result of the pinacoline rearrangement, and the less stable ketone should be converted to the more stable ketone isomeric with it. This idea had been confirmed by him previously together with A. A. Chilingaryan [28] using phenyl isopropyl ketone, which was isomerized to unsymmetrical methylphenylacetone, as an example.

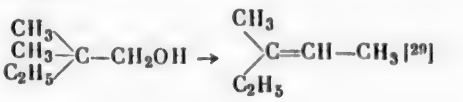


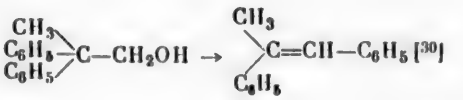
The latter compound was obtained by Tiffeno as a result of pinacoline rearrangement:

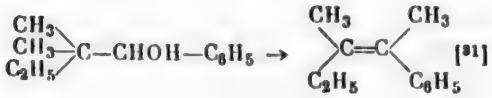


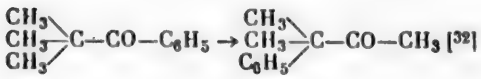
From this work by A. E. the significance of the stability of the end product for the result of the rearrangement process is clearly evident. Through this work also a new type of molecular rearrangement of a ketone to a ketone was discovered. Later this type of rearrangement was confirmed by a number of other investigations by A. E. and his co-workers. These studies indicated the deficiency of the affinity theory in explaining the mechanism of the rearangements under consideration.

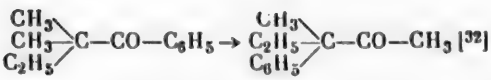
Proceeding from the idea of the mutual effect of the radicals entering into the molecule, A. E. in a series of investigations also showed the deficiency of the theory of the migrational capacity of the radicals. For this purpose he and a number of collaborators carried out studies of the molecular rearrangements of compounds containing a tertiary radical with two similar groups. In this work it appeared that in all cases a shift in the position of one of the similar radicals takes place.

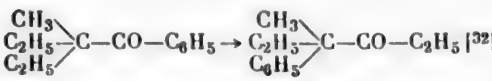


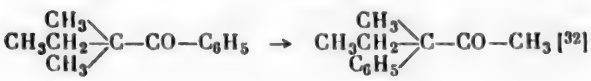






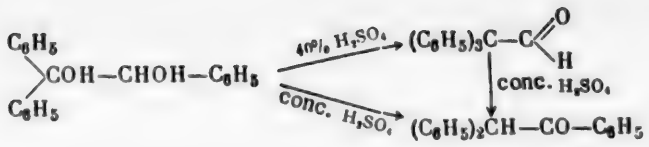






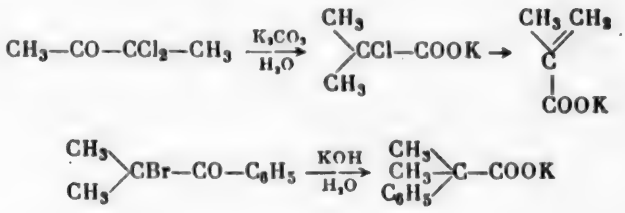
From these examples it is clearly seen that it is impossible to establish any series of migrational capacity or mobility of the radicals. A. E., approaching the consideration of these conversions with his characteristic breadth and depth of thought, regarded it as impossible to explain the mechanism of conversion solely by the properties of the radicals and thought that the effect of the reaction conditions, the internal structure of the molecule as a whole, the influence of the radicals on one another, and other factors determined and directed the processes of the conversions.

The field of isomeric conversions and molecular rearrangements of carbonyl and hydroxycarbonyl compounds and haloketones was further fruitfully and broadly developed in numerous investigations by S. N. Danilov and É. D. Venus-Danilova. The latter authors found their own original directions of investigation and a path that was new in principle. They turned their attention, for the first time, to showing experimentally that the direction of molecular rearrangements depends on the nature of the reagent that is acting and the conditions under which the rearrangement takes place. They showed that aldehydes formed from α-glycols under mild conditions are converted under more severe conditions to ketones [33].



From this basis S. N. Danilov conceived the idea of the possibility of the isomerization of a ketone to a ketone, which was later also accomplished in the work of A. E. Favorskii and A. A. Chilingaryan [28] already referred to. The investigations on the isomeric conversions of aldehydes to ketones and of ketones to isomeric ketones have great theoretical significance and should be adopted in dealing with various processes taking place at high temperatures in the presence of salt catalysts.

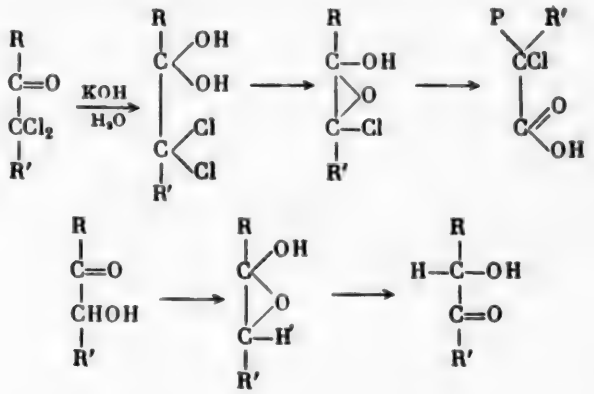
A. E. discovered a molecular rearrangement that occurs when α,α-dihaloketones and α-monohaloketones are heated with aqueous alkalies [34].



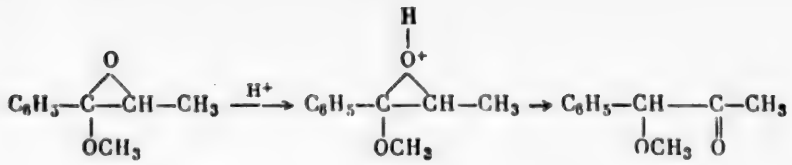
This rearrangement has been designated as the "Favorskii rearrangement" in the world literature. It makes it possible to start with ketones and prepare acids with the same number of carbon atoms.

The Favorskii rearrangement was extended by S. N. Danilov to α-haloaldehydes to yield desonic acids. Acids of the steroid group are now prepared by this route.

The investigations by A. E. of isomeric conversions and molecular rearrangements of oxygen-containing compounds constitute a broad field. In these studies of his, A. E. successfully employed schemes in which he assumed the intermediate formation of intramolecular and intermolecular addition compounds [35].



He interpreted the benzil rearrangement process in a manner similar to the acid conversion of haloketones. By means of kinetic investigations and the use of labeled atoms, the correctness of A. E's. assumption that an addition product of alkali to the carbonyl group is formed in the first phase was proved. The question of the possibility of the independent existence of α-alcohol oxide rings remained open. In 1949 T. I. Temnikova and E. N. Kropacheva [36] provided an answer to this question after they had succeeded for the first time in obtaining ethers of α-alcohol-oxides and studying their properties. It was shown that these compounds actually are isomerized in acid medium with the migration of hydrogen to a neighboring position.



A. E's. widely developed idea of the intermediate formation of mobile cyclic and pseudocyclic forms has proved fruitful. At the present time intermediate forms of this type are assumed for the interpretation of various kinetic and stereochemical data in investigations of oxygen containing organic compounds.

A. E'. research proceeded in many fields of organic chemistry; his investigations were varied in purpose and objectives, very comprehensive, and executed on a high theoretical and experimental level. They were permeated by a single purpose and a single idea—how to reveal more deeply the essence of natural phenomena, explain the mechanism of chemical processes and conversions, and understand the molecule in its movement in chemical conversions. In addition to the important theoretical significance of A. E's. investigations, they revealed the possibility of accomplishing the commercial manufacture of technically valuable products—dioxane, acrylates, vinyl ethers and acetaldehyde, adhesives and valuable pharmaceutical agents, high-molecular compounds, in particular synthetic rubber, etc. There is no doubt that in the future the research accomplishments of A. E. will be a stimulus and a resource for ever newer discoveries in the field of theoretical organic chemistry and chemical industry.

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ISOMERIZATION OF HYDROXYALDEHYDES

XV. ACID CONVERSION OF GLYCERALDEHYDE AND ITS HALOGENATED DERIVATIVES

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In the acid conversion of α-monohalo- and α-monohydroxyaldehydes, according to the investigations of S. N. Danilov and É. D. Venus-Danilova [1, 2], the aldehyde group becomes a carobyxyl and an atom of hydrogen appears on the neighboring carbon atom in place of the halogen or hydroxyl group. This sort of conversion should be numbered among the reactions of intramolecular oxidation-reduction [3].

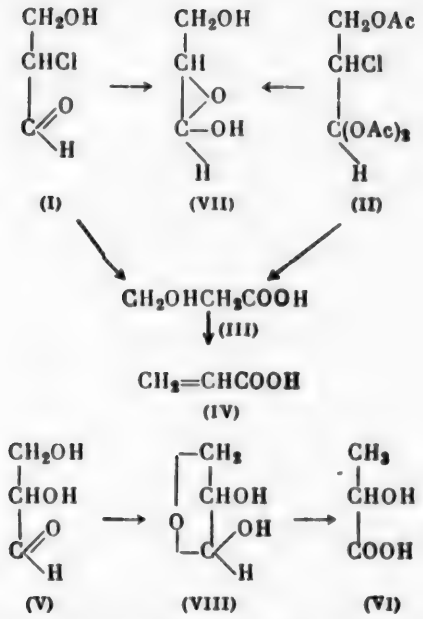
The acid conversion of α-monohalo- and α-monohydroxyaldehydes takes place with very high yields in the presence of lead, copper, or mercury hydroxide, where the amount of isomeric α-hydroxyketones, which are formed in weakly alkaline medium, is decreased and the Cannizaro reaction does not occur.

It is known that in the acid conversion [4] of di- and monohaloketones (Favorskii reaction), in contrast to the monohaloaldehydes, a rearrangement of the skeleton of the molecule usually is observed [5]. Until now the conversion of the α-hydroxyketones themselves, in contrast to the α-hydroxyaldehydes, into acids has not been observed. The acid conversion of α-monohydroxyaldehydes may be referred to as their saccharic rearrangement, since it has characteristics in common with the saccharic rearrangement of monoses (aldoses and ketoses). But the formation of saccharic acids from monoses takes place not so much with the participation of alcohol groups neighboring to the carbonyl groups, as in the case of the monohydroxyaldehydes, as at the expense of more distant alcohol groups.

It has been suggested [6] that, depending on the participation of different alcohol groups in the rearrangement, 12 different structural isomers of the saccharic acids can exist, but as yet the formation of only 3 isomers has been reliably disclosed by experiment (stereoisomeric saccharic, isosaccharic, and metasaccharic acids); probably a fourth structural isomer also—parasaccharic acid. A fifth type of saccharic acid, orthosaccharic or desonic, has been obtained [6] from 2-halomonoses by the action of lead hydroxide.

It can be assumed that monoses in the molecules of which the other hydroxyl groups are replaced by alkali-stable substituents, while the hydroxyl groups on the first and second carbon atoms remain unsubstituted, will be isomerized to desonic acids by the action of the hydroxides of the heavy metals, as the 2-halogenated aldehydes are.

Our experiments showed that while (D + L)-glyceraldehyde itself (V) is isomerized by the action of lead hydroxide to lactic (α-hydroxypropionic) acid (VI), its 2-monohalogenated derivatives (I, II) form 3-hydroxypropionic (hydroacrylic) acid (III), which is converted further into acrylic acid (IV).

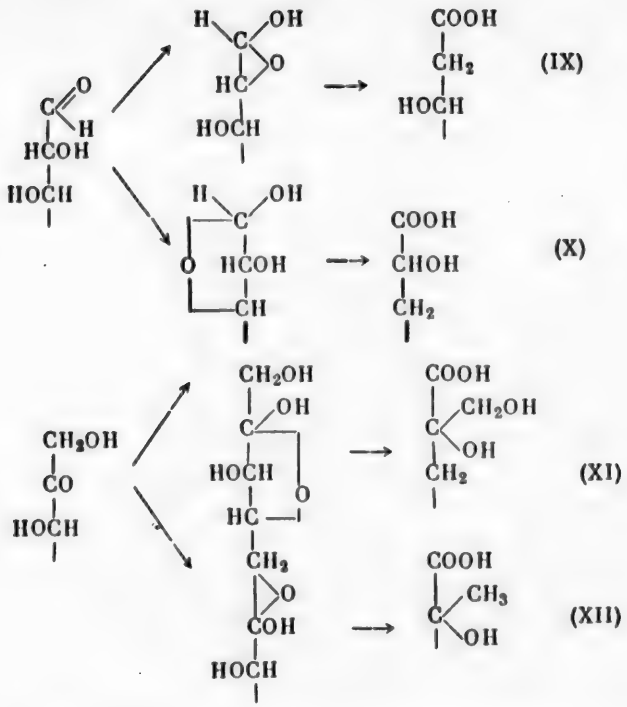


These conversions show that the halogen atom located in the α-position to the aldehyde group participates in the oxidation-reduction conversion of the α-halogenated derivatives of glyceraldehyde. The reaction can be written as occurring by way of the α-alcohol-oxides (VII), widely employed by A. E. Favorskii in interpreting the conversions of halogenated and hydroxyketones. The oxidation-reduction conversion of glyceraldehyde takes place between the aldehyde group and the β-alcohol group with the formation of lactic acid (the simplest saccharic acid), in the same way that the alcohol groups more distant from the aldehyde group are reduced in the aldoses in the saccharic rearrangement. The conversion of glyceraldehyde to lactic acid can be graphically represented via the β-alcohol-oxide (VIII).

There are data [7] indicating that D-glucose (1-C^{14}), when acted on by 3 N potassium hydroxide solution at 50°, forms lactic acid labeled on C_1 and C_3.

There is a report [8] that D-glyceraldehyde labeled in the primary alcohol group, $C^{14}H_2OH$, is isomerized to lactic acid by the action of 1.68 N sodium hydroxide solution with distribution of the radioactivity almost equally at C_1 and C_3. When lime water is used as the reagent, D-glyceraldehyde forms lactic acid with the radioactivity also predominantly in the methyl and carboxyl groups, with the preponderance of it in the methyl group.

These data can be recognized as being in agreement with the β-alcohol-oxide mechanism, by means of which we represented the saccharic rearrangement of (D + L)-glyceraldehyde. In the literature [8] the formation of lactic acid from D-glucose is explained through the dienol and methylglyoxal. The formation of saccharic acids from monoses can be represented as going through the α- and β-alcohol-oxides, and in the aldoses, as also in unsubstituted glyceraldehyde, it is predominantly the β-alcohol groups that participate in the oxidation-reduction conversion when the saccharic acids are formed, while the formation of desonic acids (IX) from the 2-halogenated monoses is graphically represented via the α-alcohol-oxides. Without entering into a discussion of the data on the saccharic acids and the mechanisms proposed in the literature, let us note the following facts: 1) The isomerization of the aldoses to metasaccharic acid can be represented as going through the β-alcohol-oxide compounds (X); 2) the formation of isosaccharic acid possibly takes place with the participation of the β-alcohol-oxides of the ketoses (XI) with a shift of a hydrogen atom to the β-position; 3) to write the formation of saccharic acid from ketoses through the α-alcohol-oxide (XII); 4) if the structure of parasaccharic acid is confirmed, its formation from 3-ketohexose can be represented through the <2,3> alcohol-oxides with a shift of the CH_2OH-CH< group to the fourth carbon atom.



Further investigation is necessary to confirm the formation of saccharic acids through the α- and β-alcohol-oxide (glucoside) compounds of the aldoses and ketoses, the existence of which in alkaline media is quite probable. The formation of β-hydroxypropionic acid from halogen derivatives of glyceraldehyde through the α-alcohol-oxide, and of lactic acid from glyceraldehyde itself through the β-alcohol-oxide seems to be the only probable mechanism, in the light of present knowledge.

EXPERIMENTAL

The acid conversion of (D,L)-glyceraldehyde and of its halogen and haloacetyl derivatives was carried out in our experiments by heating with freshly precipitated lead hydroxide to eliminate possible side reactions (hydroxyketone conversion, condensation, and cleavage) that take place in more strongly alkaline media.

1. Acid Conversion of 1,1,3-Triacetyl-2-chloropropanal (II) (From the experiments of A. N. Anikeeva)

The synthesis of the starting material, 1,1,3-triacetyl-2-chloropropanal (II), was carried out under the conditions described in a previous article [9], by chloroacetylation of acrolein diacetate. In the first experiments, 20 g of 1,1,3-triacetyl-2-chloropropanal (b.p. 117-118° at 1 mm, n^{20}_D 1.4424) was heated with an excess of lead hydroxide (45 g in 150 ml of water) on a water bath with a gradual elevation of the temperature to 95° in the course of several hours, until the reaction for chlorine in an ether extract was negative. The reaction mixture took on a brown color upon long heating. The precipitate of lead chloride and excess lead hydroxide was filtered off. The ether contained no neutral products, since no unreacted starting material remained. After the water had been distilled off from the reaction mixture in vacuum, a mixture of lead salts was obtained. Although in the reaction the lead salt of hydracrylic acid was formed, in addition to a large amount of lead acetate, it was difficult to separate the former from the mixture of salts. The presence of hydracrylic acid in the reaction products was demonstrated by converting it to acrylic acid, which was characterized as its methyl ester.

Anhydrous methyl alcohol was poured over the lead salts and part of the salts went into solution. Sulfuric acid was added gradually to the mixture until a pH of 5 was reached, while heating up of the solution was avoided. Then the mixture was heated to slight boiling for 2 hours and left for 12 hours at room temperature. The precipitate of lead sulfate was filtered off and the filtrate was fractionally distilled. Part of the product was isolated in the form of a polymer of methyl acrylate. After the excess methyl alcohol and methyl acetate had been distilled

off, a fraction with b.p. 81-84°, $n^{20}D$ 1.3981, was obtained. The material reacted readily with bromine, which confirmed the presence of a double bond in the product. Analysis and physical constants confirmed that the fraction obtained was actually methyl acrylate.

Found %: C 55.80, 55.99; H 7.21, 7.44, $C_4H_6O_2$. Calculated %: C 55.81; H 6.97.

2. Acid Conversion of 2-Chloro-3-hydroxypropanal (I) (From the experiments of A. A. Lopatenok)

The synthesis of this chlorohydrin from acrolein and hypochlorous acid, in contrast to data in the literature [10], was carried out with hypochlorous acid prepared not from sodium hypochlorite and hydrochloric acid, but directly with freshly precipitated mercuric oxide. In the latter case, in our experiments 2-chloro-3-hydroxypropanal was obtained free of contamination by dichloride. A 3-4% solution of hypochlorous acid, stable for long periods, was added according to calculation to a mixture of acrolein (b.p. 52°, $n^{20}D$ 1.3966) and water. Then the solution was neutralized with sodium hydroxide and the water was distilled off in vacuum at 50°. After the material had been dried in a vacuum desiccator, it was obtained as a clear, thick, slightly yellowish sirup (yield 72%). A purer product was obtained when the solution was not neutralized, but the excess hypochlorous acid and the colored contaminants were removed with the ion-exchange resin ÉDÉ-10. The constants of the compound were $n^{20}D$ 1.5036, d_{20}^{20} 1.4477, MR_D 22.18. $C_3H_5O_2Cl$. Calculated 22.46.

The analysis for chlorine was close to theoretical.

2-Chloro-3-hydroxypropanal was soluble in water, alcohol, dioxane, and acetone, but insoluble in diethyl ether. Care was necessary in distilling 2-chloro-3-hydroxypropanal, since the compound decomposed easily and polymerized on distillation to a solid product (softening point about 60°).

A freshly prepared solution of 2,4-dinitrophenylhydrazine in a mixture of alcohol and sulfuric acid was added to an alcohol solution of 2-chloro-3-hydroxypropanal, and the mixture was heated for 10 minutes on a boiling water bath. A yellow-red precipitate, containing no chlorine, immediately separated out. After this material was washed with alcohol, it melted at 284-285°, which agreed with the 2,4-dinitrophenylhydrazone of glyceraldehyde. A mixed sample with the 2,4-dinitrophenylhydrazone prepared directly from glyceraldehyde showed no depression in melting point. The identity of these 2,4-dinitrophenyldrazones indicated that 2-chloro-3-hydroxypropanal actually was obtained by the action of hypochlorous acid on acrolein.

The chlorine atom in 2-chloro-3-hydroxypropanal is not hydrolyzed especially easily. Thus, when aqueous solutions of this compound were heated with freshly precipitated barium carbonate, hydrolysis to glyceraldehyde required prolonged heating to 100-120° for 10 hours or more.

The oxidation-reduction conversion of 2-chloro-3-hydroxypropanal to β-hydroxypropionic acid took place upon heating the former with freshly prepared lead hydroxide. In some experiments lead nitrate was used with the calculated amount of sodium hydroxide, which unnecessarily contaminated with byproduct salts the desired salts, which were obtained in purer form by the oxidation-reduction conversion of the 2-chloro-3-hydroxypropanal in the presence of previously prepared lead hydroxide that had been well washed. In the presence of lead hydroxide, an aqueous solution of 2-chloro-3-hydroxypropanal was almost completely converted to salts by heating to 100-120° for 3 hours (cessation of Beilstein test for chlorine). After the lead chloride had been removed from the reaction mixture and the water had been distilled off in vacuum, the salts were treated with hot acetone. Only a very small amount of neutral, nonhalogen material (0.1 g from 10 g of 2-chloro-3-hydroxypropanal), probably glyceraldehyde, went into the acetone. The salts obtained did not dissolve in alcohol, even hot.

To isolate the organic acid, the aqueous solution of lead salts was passed through a cation exchange resin (KU-2), and then an anion exchange resin to remove the chlorine ion (sometimes also nitric acid). The lead salt obtained from these acids (through lead carbonate) was precipitated from aqueous solution with organic liquids (anhydrous acetone, alcohol, dioxane). When dried by heating, the salt liquefied and turned dark; therefore the drying was done in a vacuum desiccator at room temperature.

In some experiments, preliminary purification was carried out with silver oxide to remove the chloride ion and then the lead ion was removed with only a cation exchange resin. When we tried to distill the acid with water, acrylic acid went over into the distillate because of the decomposition of the hydracrylic (β-hydroxypropionic) acid first formed. The experiments showed that in the presence of lead hydroxide the chlorohydrin of

glyceraldehyde yielded almost quantitatively the salts of an organic acid, with the absence, or only very small amounts of neutral products, in contrast to what was observed when 2-chloro-3-hydroxypropanal was heated with barium carbonate, where mainly glyceraldehyde was obtained.

The acid obtained from 2-chloro-3-hydroxypropanal was a liquid with a sharp acid odor (the result of partial transformation to acrylic acid), which proved to be hydracrylic acid. This was confirmed by analysis of the salts and conversion of the acid to acrylic acid through the methyl ester.

3. Intramolecular Acid Oxidation-Reduction of Glyceraldehyde (V) (From the experiments of A. A. Lopatenok)

The (D, L)-glyceraldehyde necessary for the experiments was prepared by a method described in the literature from 2-chloro-3-hydroxypropanal through its ethylene glycol acetal [10] and had the properties known from the literature. For the experiments we used not the dimeric crystalline glyceraldehyde but the monomeric product, in order to avoid the decrease in reactivity, with an admixture of ethylene glycol that remained in part after the decomposition of the starting acetal. The glyceraldehyde was easily converted by the usual method to the 2,4-dinitrophenylhydrazone with m.p. 284-285°. For 1 mole of glyceraldehyde we used 1.5 moles of lead hydroxide, calculated (with an excess) on the basis of the lead salt of lactic acid. The reaction was carried out in an atmosphere of nitrogen (to avoid oxidation) for 2 hours at 60° and for 1 hour on a boiling water bath with stirring. In other cases the heating was continued for 7 hours at 60°. The excess of lead hydroxide was removed by a current of carbon dioxide. After removal of the precipitate, the solution was concentrated in vacuum at 50°. A thick brown mass remained. About 60% of the glyceraldehyde used in the reaction was converted to the lead salt, which precipitated as a white powder upon dilution with alcohol (but not with acetone); part of the glyceraldehyde did not enter into the reaction and was extracted by the alcohol.

Salts were obtained, and also derivatives with the properties described in the literature for lactic acid and its salts. This confirmed the oxidation-reduction conversion of the glyceraldehyde to lactic acid.

SUMMARY

1. While glyceraldehyde itself is isomerized in the presence of lead hydroxide to lactic acid, its 2-monochloro derivatives under similar conditions form β-hydroxypropionic (hydracrylic) acid.

2. The formation of hydracrylic acid is explained as occurring through the α-alcohol-oxide and that of lactic acid through the β-alcohol-oxide compounds.

3. The formation of saccharic acids from monoses is explained by the mobility of the hydrogen atom of the α- and β-alcohol groups and radicals through the α- and β-alcohol-oxide compounds.

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CYCLOHEXYLIDENE-D-XYLOSE•

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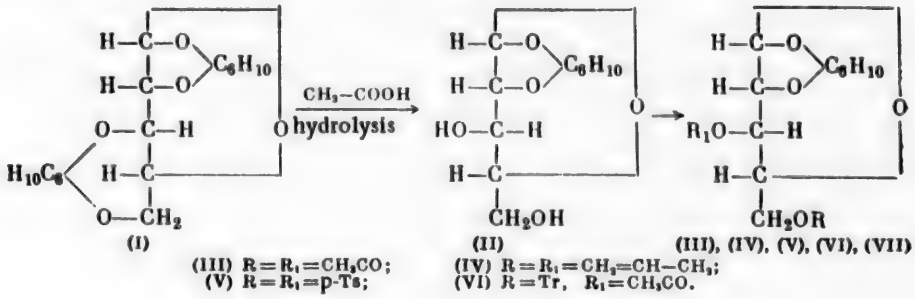
Crystalline dicyclohexylidene-D-xylose has been described previously [1], but its structure has not been proved. Dicyclohexylidene-D-glucose [2], L-sorbose [3], and D-mannose [4] have a furanose structure. Our experiments indicate that dicyclohexylidene-D-xylose also is a furanose.

The problem in the present investigation was the hydrolysis of dicyclohexylidene-D-xylose (I) and the synthesis of derivatives. The hydrolysis was carried out with 70% acetic acid at room temperature and with heating, and also with hydrochloric acid dissolved in methyl alcohol. Crystalline 1,2-cyclohexylidene-D-xylose (II) was isolated and the following derivatives were synthesized: diacetylcyclohexylidene-D-xylose (III), diallyl-cyclohexylidene-D-xylose (IV), ditosylcyclohexylidene-D-xylose (V), and tritylacetylcyclohexylidene-D-xylose (VI). The synthesis of tritylacetylcyclohexylidene-D-xylose showed that cyclohexylidene-D-xylose contains a free primary hydroxyl group.



(I) (II) (III), (IV), (V), (VI), (VII)

(III) R = R₁ = CH₃CO;
(V) R = R₁ = p-Ts;
(IV) R = R₁ = CH₂=CH–CH₂;
(VI) R = Tr, R₁ = CH₃CO.

EXPERIMENTAL

Hydrolysis of dicyclohexylidene-D-xylose (I) with 70% acetic acid. a) At room temperature 3.1 g of dicyclohexylidene-D-xylose was dissolved in 50 ml of 70% acetic acid and left to stand at room temperature for 72 hours. The optical rotation was measured periodically in a one-decimeter tube, and a test with Fehling's solution also was made. The initial rotation $\alpha^{18}D$ was + 0.9 and the final rotation was + 0.1. Then the solvent was distilled off under reduced pressure at 50°. The residue was washed with petroleum ether to remove unchanged starting material. Further purification was accomplish by crystallization from benzene. M. p. 83-84°. The yield of 1.2-cyclohexylidene-D-xylose (II) was 1 g (43%).

b) Eighteen grams of dicyclohexylidene-D-xylose was dissolved in 300 ml of 70% acetic acid with heating, and the solution was heated for 20 minutes on a water bath at 60-70°. The solvent was quickly distilled off under

• The present communication is the fourth of the series "Cyclohexylidene compounds of monoses and polyatomic alcohols."

reduced pressure at 50°. There were sirup and crystals in the residue. The crystals were separated from the sirup and after crystallization from alcohol 7.8 g (52%) of 1,2-cyclohexylidene-D-xylose was obtained with m.p. 78-79°. After the compound was dried it had m.p.83-84° $[\alpha]^{18}D$-20° (in methanol, c 2.1).

Found %: C 57.15, 57.54, H 8.01, 7.87. $C_{11}H_{18}O_5$. Calculated %: C 57.39; H 7.82.

Hydrolysis of dicyclohexylidene-D-xylose with hydrochloric acid in methyl alcohol solution. Samples of 1.5 g of dicyclohexylidene-D-xylose each were placed in 10 small flasks and dissolved in methyl alcohol by heating slightly on a water bath, then 0.5 ml of concentrated hydrochloric acid was added to each sample and the volume made up to 50 ml in a graduated flask. At certain time intervals (1, 2, 3, 4, 5, 6, 7, 9, and 24 hours) the rotation was measured and the reaction mixture was neutralized with a concentrated solution of sodium hydroxide in the presence of phenolphthalein and the methanol was distilled off under reduced pressure. The hydrolysis product was recrystallized twice from benzene. The crude product melted at 78-79°. The product after drying melted at 83-84°.

Hydrolysis time (in hr)	Yield of 1,2-Cyclohexylidene-D-xylose (in %)
1	22.7
2	29
3	38.0
4	59.02
5	57.0
6	51.9
7	51.9
8	—
9	50.4
24	0

The monocyclohexylidene-D-xylose crystallized in platelets, did not react with Fehling's solution, dissolved upon heating in benzene, alcohol, and water, and was difficultly soluble in petroleum ether.

The yield of monocyclohexylidene-D-xylose 1, 2, 3, 4, 5, 6, 7, 9, and 24 hr after hydrolysis is given in the table.

The data show that the largest yield of 1,2-cyclohexylidene-D-xylose was obtained after 4 hours hydrolysis of the dicyclohexylidene-D-xylose; then further hydrolysis takes place with the formation of xylose.

The change in the angle of rotation in a two-decimeter tube after the above-mentioned time intervals is shown in the figure.

3,5-Diacetyl-1,2-cyclohexylidene-D-xylose (III). To a solution of 1.1 g of 1.2-cyclohexylidene-D-xylose in 7 ml of anhydrous pyridine was added 5.1 ml of acetic anhydride and 0.6 g of anhydrous sodium acetate. The mixture was shaken for 15 minutes and then left at room temperature. After 24 hr the mixture was poured into 50 g of water and ice. An oil separated out; this was triturated with ice until the odor of pyridine disappeared. The thickened mass was dissolved in ether and dried with sodium sulfate. After the solvent had been evaporated off, a sirup remained, which was distilled in vacuum at 175° (1 mm). Yield 0.7 g (45%), $[\alpha]^{18}D$ + 31.6° (in methanol, c 4.66).

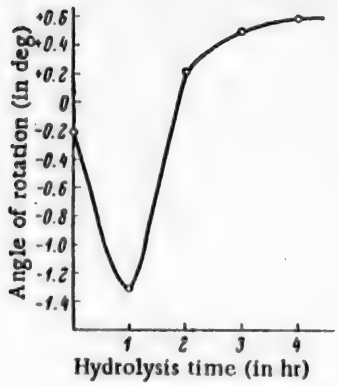
Found %: C 57.00; H 7.18. $C_{15}H_{22}O_7$. Calculated %: C 57.32; H 7.36.

1,2-Cyclohexylidene-3,5-diallyl-D-xylose (IV).• Seven grams of allyl bromide was added to 5.2 g of 1,2-cyclohexylidene-D-xylose in a three-necked flask connected with a dropping funnel, reflux condenser, and mechanical stirrer. The well-stirred reaction mixture was kept at 70°. A solution of 3 g of sodium hydroxide in 5 ml of water was added slowly over the course of 5 minutes and stirring was continued for 30 minutes. Then 5.5 ml of water was added and the unsaturated, readily volatile ingredients were distilled off on a water bath. Then the mixture was extracted with ether, the ether extract was washed with water and dried with sodium sulfate, and the ether was distilled off on a water bath. A brown liquid remained, which was distilled in vacuum in an atmosphere of carbon dioxide gas at 198-199° (3 mm). A light yellow, thick, sirupy liquid was obtained, which was immiscible with water. The substance decolorized bromine water and dissolved in benzene, ether, and ethanol.

d_4^{20} 1.1151, $n^{20}D$ 1.4805, $[\alpha]^{19}D$-26.3° (in methanol, c 1.8).

Found %: C 65.58, 65.67; H 8.32, 8.42. $C_{17}H_{26}O_5$. Calculated %: C 65.80; H 8.48.

•In the synthesis of (IV) a method was used that was given in the literature [5] for the synthesis of other allyl ethers of monoses.



3,5-Ditosyl-1,2-cyclohexylidene-D-xylose (V). This compound was synthesized by the method for preparing the tosyl ether of glucose which was described by S. N. Danilov and I. S. Lishanskii [6]. To a solution of 0.52 g of 1,2-cyclohexylidene-D-xylose in 5.5 ml of anhydrous pyridine was added 2.44 g of p-tosyl chloride. The mixture stood at room temperature for 4 days, then was decomposed with ice water. The crystals that precipitated were washed with water, 5% hydrochloric acid, and again with water, and dried in the air. M. p. 134° (from acetone). Yield 1.82 g (80%). $[\alpha]^{17}D$-24.7° (in methanol, c 1.28).

Found %: S 11.76. $C_{25}H_{30}O_9S_2$. Calculated %: S 11.85.

6-Trityl-3-acetyl-1,2-cyclohexylidene-D-xylose (VI). A solution of 1.3 g of cyclohexylidene-D-xylose in 6 ml of anhydrous pyridine and 1.4 g of trityl chloride stood at 40°. After 16 hours, 0.4 g of anhydrous sodium acetate was added and the reaction mixture was left at the same temperature for 8 hours, then cooled to 0°, 4 ml of acetic anhydride and 0.4 g of anhydrous sodium acetate were added, and the mixture again stood at room temperature for 16 hours. After this the contents of the flask were poured into 600 g of ice. A precipitate separated out, and was filtered off and carefully washed with ice water. The crude product (2.4 g) contained an admixture of triphenylcarbinol. After treatment with ether and 3 crystallizations from methanol, 1.36 g (53%) of(VI) was obtained with m.p. 70-71°. The compound was soluble in ether and acetone and somewhat more difficultly soluble in methanol and ethanol.

Found %: C 74.57; H 6.70. $C_{32}H_{34}O_6$. Calculated %: C 74.70; H 6.61.

SUMMARY

1. The hydrolysis of dicyclohexylidene-D-xylose was carried out by two methods: with 70% acetic acid and with hydrochloric acid dissolved in methanol.

2. 1,2-Cyclohexylidene-D-xylose, 3,5-acetyl-1,2-cyclohexylidene-D-xylose, 3,5-diallyl-1,2-cyclohexylidene-D-xylose, and 3,5-ditosyl-1,2-cyclohexylidene-D-xylose were isolated and characterized.

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SYNTHESIS AND INVESTIGATION OF THE CONVERSIONS OF ACETYLENIC α-GLYCOLS WITH FREE ACETYLENIC HYDROGEN

III. SYNTHESIS OF METHYLETHYLISOPROPYLETHYLENE GLYCOL AND METHYLETHYNYL-n-PROPYLETHYLENE GLYCOL AND THEIR CONVERSION UNDER THE INFLUENCE OF SULFURIC ACID TO SUBSTITUTED TETRAHYDROFURANONES

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A. E. Favorskii and É. D. Venus [1], and later É. D. Venus-Danilova et al. [2] studied the conversions of a number of pinacols with substituted acetylenic radicals and showed that in acid medium these glycols are capable of undergoing two kinds of isomeric conversions—pinacoline and acetylene-allene rearrangements; in some cases dehydration takes place with the formation of an enyne alcohol. The direction of the reaction and the ratio of the products formed depend on the nature and arrangement of the radicals that enter into the makeup of the glycol.

Few pinacols containing unsubstituted acetylenic radicals are known. A. E. Favorskii and A. S. Onishchenko [3] prepared several pinacols of the type:

$$R-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-C\equiv CH \qquad R = CH_3,\ C_2H_5,\ C_3H_7.$$

Similar pinacols have been obtained by the condensation of keto alcohols with acetylene in the presence of sodamide [4], but the authors did not make a study of the conversions of these glycols. Favorskii and Onishchenko [5] investigated the reaction of trimethylethynylethylene glycol with concentrated sulfuric acid and showed that in this process a pinacoline rearrangement took place with subsequent hydration of the triple bond and that dimethylacetylacetone was formed.

One of us together with A. N. Shirshova [6] studied the reaction of dimethylethynylphenylethylene glycol with dilute sulfuric acid, in which, apparently, an acetylene-allene rearrangement takes place with subsequent cyclization and resinification of the hydroxyaldehyde produced. In work with O. A. Zakhar'evskaya [7] we showed that as a result of the reaction of dimethylethynylisobutylethylene glycol with dilute sulfuric acid, dehydration takes place with the formation of an enyne alcohol.

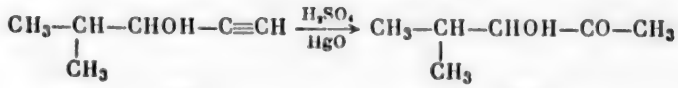
Primary-tertiary and secondary-tertiary α-glycols with substituted acetylenic radicals were studied by L. . . Pavlova and É. D. Venus-Danilova together with V. M. Al'bitska. In the first case [8], when an alcoholic solution of sulfuric acid reacted with the compounds, the partial ether of the starting glycol and 2, 4-diphenylfuran was obtained, and in the second case [9] a compound containing a carbonyl group was obtained, which was readily enolized. The conversion of these glycols into furans take place on reaction with an alcoholic solution of mercuric chloride [8, 10].

Secondary-tertiary α-glycols with unsubstituted acetylenic hydrogen have not been studied up to the present time.

In the present work we synthesized two secondary-tertiary α-glycols with unsubstituted acetylenic hydrogen—methylethynylisopropylethylene glycol (VI) and methylethynyl-n-propylethylene glycol (XI) and studied their reaction with sulfuric acid. The synthesis of the glycols was carried out in three stages: the synthesis of the secondary acetylenic alcohol, the hydration of this compound to the corresponding keto alcohol, and the condensation of the keto alcohol with acetylene to form the glycol.

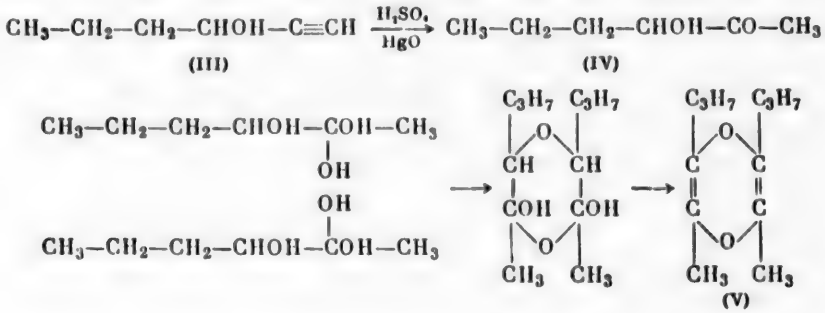
The starting materials for the synthesis of the acetylenic alcohols were isobutyric and butyric aldehydes. The condensation of the aldehydes with acetylene by the method of A. E. Favorskii gives low yields of the secondary alcohols as a result of the ease of condensation of the aldehydes. I. A. Favorskaya [11] modified this method and considerably increased the dilution of the reaction mixture with ether and the duration of the reaction, thus raising the yield of the secondary alcohols to 60-65%. A similar increase in yield was obtained by I. N. Nazarov [12], who carried out the condensation of aldehydes with acetylene in an autoclave. McGrew and Adams [13] carried out the condensation of ketones and aldehydes with acetylene in the presence of sodamide in liquid ammonia. We used both the method of I. A. Favorskaya and that of McGrew and Adams for the synthesis of our alcohols. In the case of isobutyraldehyde in both instances the acetylenic alcohol was obtained in 73% yield, and in the case of butyraldehyde the yield of the alcohol by the first method was 47-53%, and by the second method it was 30%.

When isopropylethynylcarbinol (I) was hydrated by the method of Kucherov the keto alcohol isopropylacetylcarbonyl (II) was obtained in 76% yield and gave the corresponding 2,4-dinitrophenylhydrazone.



(I) (II)

When n-propylethynylcarbinol (III) was hydrated, the keto alcohol n-propylacetylcarbinol (IV) was obtained only in 30% yield and also formed the corresponding 2,4-dinitrophenylhydrazone. In this reaction the formation of a byproduct occurred as a result of the condensation of two hydrated molecules of propylacetylcarbinol, from which 4 molecules of water then split out:



(III) (IV) (V)

The structure of product (V) cannot be considered strictly proved, but it seems to us most probable on the basis of the properties and analysis of this compound. This compound does not contain a carbonyl and hydroxyl group and it does not give a reaction for acetylenic hydrogen or decolorize a solution of potassium permanganate; an attempt to hydrogenate it was not successful. The IR absorption spectrum confirmed the presence in this compound of a double bond (1664 cm^{-1}) and ether oxygen in an unsaturated ring = C-O-C= (1140 cm^{-1}) [14]. On oxidation of compound (V) with $KMnO_4$ solution, it was not possible to isolate products other than acetic acid, and consequently the arrangement of the radicals in the molecule of (V) cannot be considered established; it could correspond with equal probability to the formula of 2,6-dimethyl-3,5-dipropyldioxadiene-1,4 or that of 2,5-dimethyl-3,6-dipropyldioxadiene-1,4.

The synthesis of the acetylenic glycol 3,5-dimethylhexyne-1-diol-3,4 (VI) was carried out both by Favorskii's method, the condensation of isopropylacetylcarbinol with acetylene in the presence of KOH, and by

the reaction of this keto alcohol with sodium acetylide in liquid ammonia. In the first case the yield of glycol was 58%. Upon distillation in vacuum, part of the glycol crystallized and the rest of it remained in the form of a thick liquid, even when repeatedly distilled. A detailed study of the liquid and crystals showed that we had here two isomeric forms of the same compound, as a result of the presence in the glycol of two asymmetric carbon atoms.

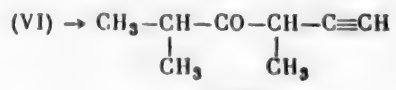
(VI)

In liquid ammonia medium the glycol was obtained in 85% yield and was obtained only in liquid form in all of the experiments.

The synthesis of the second glycol, 3-methylheptyl-1-diol-3,4 (XI) was carried out only by the reaction of propylacetylcarbinol with sodium acetylide in liquid ammonia, but in this case the yield was much lower (30-35%), and here also we obtained only the liquid form of the glycol. The two glycols readily formed precipitates of the silver derivative when acted on by an ammoniacal solution of silver oxide. The two forms of the acetylenic glycol (VI) were hydrogenated in the presence of platinum black, and the amount of hydrogen absorbed corresponded to the presence of a triple bond.

It is known that tertiary acetylenic alcohols and ditertiary acetylenic glycols are easily broken down into acetylene and ketone or acetylene and keto alcohol by heating with 10% potassium hydroxide solution. The secondary acetylenic alcohol isopropylethynylcarbinol (I) was not decomposed under these conditions, and heating with 25% alkali solution was required to break it down.

When the liquid form of the glycol (VI) was boiled with 10% sulfuric acid, almost all of the glycol was recovered from the reaction and crystallized on distillation. When the glycol (VI) was heated with 20% sulfuric acid, a pinacoline rearrangement took place with a shift of the hydrogen of the secondary alcohol group.

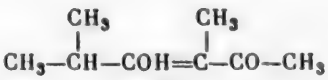


(VIII)

The 3,5-dimethylhexyn-1-one-4 (VIII) obtained formed a precipitate of silver derivative, did not contain a hydroxyl, and gave a 2,4-dinitrophenylhydrazone.

When the glycol (VI) was treated with concentrated sulfuric acid at -10° (Onishchenko's conditions) [5], we obtained two compounds: mesityl oxide (VII) (15.8%) and a cyclic enol, 3-methyl-2-isopropyl-4-hydroxydihydrofuran-2,5 (IX) (44%). This compound did not contain acetylenic hydrogen, gave no precipitate with 2,4-dinitrophenylhydrazine, reacted with CH_3MgI, decolorized potassium permanganate solution, and colored an alcoholic solution of ferric chloride an intense violet.

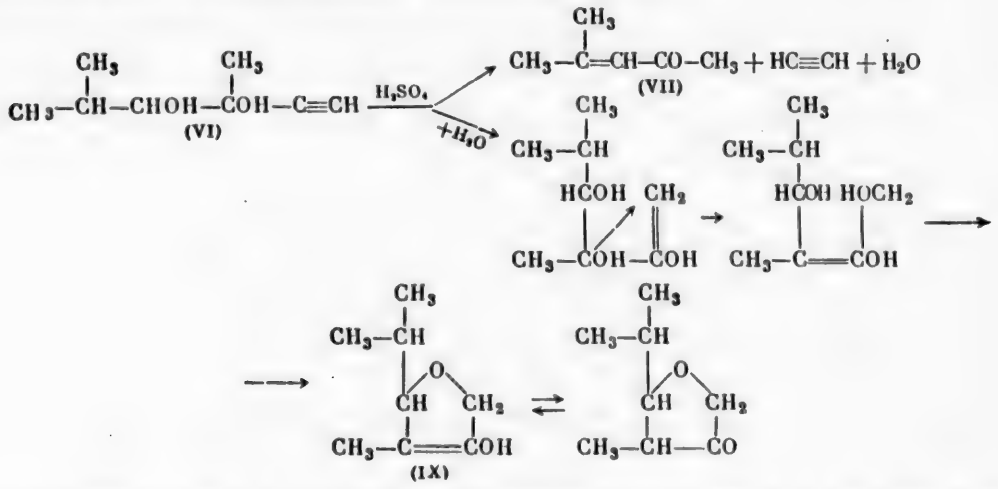
When we reacted the glycol (VI) with concentrated sulfuric acid, we expected to obtain the enol 2,4-dimethylhexen-3-ol-3-one-5 (X) as a result of the splitting out of a molecule of water and hydration of the triple bond.



(X)

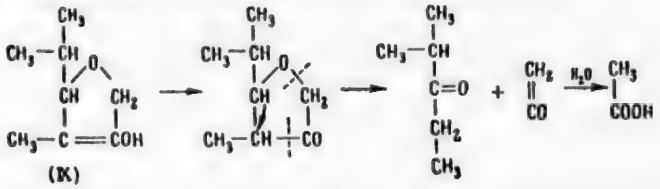
An enol of such a structure, however, would be easily hydrogenated and would give a 2,4-dinitrophenylhydrazone; the enol that we obtained did not react with 2,4-dinitrophenylhydrazine and was not hydrogenated under the usual conditions in the presence of platinum black, which indicated that the double bond in the molecule of the dihydrofuran was in the 3,4-position; such a bond is considerably more inert than one in the 2,3-position. The structure of the enol was confirmed by the IR spectrum: absorption bands for a carbonyl (1698 cm^{-1}), a double bond (1650 cm^{-1}), and an ether oxygen in a tetrahydrofuran ring (1075 cm^{-1}) were found. The enol

content of the keto-enol mixture was determined by Meyer's method [15] and amounted to 17%. The formation of the two reaction products can be represented by the following diagram:



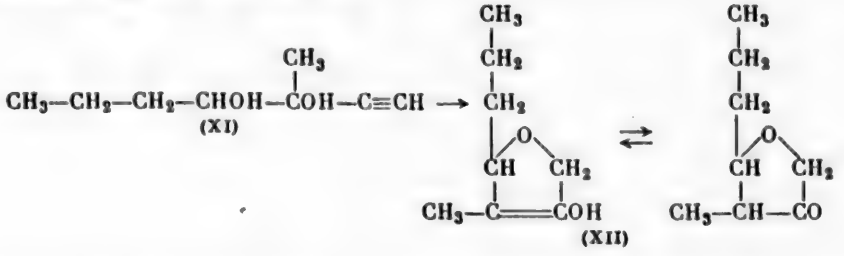
Compound (IX)—3-methyl-2-isopropyl-4-hydroxydihydrofuran-2,5—proved to be very stable in acid medium: It did not react either with concentrated hydrochloric acid or with dry hydrogen chloride and was recovered unchanged after heating with acetic anhydride.

The enol (IX) was very easily cleaved by the action of the alkaline agents that we employed (Na in liquid ammonia, sodium ethylate, 20% potassium hydroxide solution) with the formation of ethyl isopropyl ketone and acetic acid. To explain this reaction, the following mechanism can be assumed.



The ketene formed immediately hydrolyzes to acetic acid. The structure of the ketone was demonstrated by reverse synthesis and by the preparation of a 2,4-dinitrophenylhydrazone that gave no depression in melting point when mixed with a sample of known ethyl isopropyl ketone.

When 3-methylheptyne-1-diol-3,4 (XI) was reacted with concentrated sulfuric acid at -10°, only one product was obtained—the cyclic enol (XII) 3-methyl-2-propyl-4-hydroxydihydrofuran-2,5—in the form of a keto-enol mixture containing 28% of the enol form.



The properties of the hydroxydihydrofuran (XII) agreed completely with the properties of its homolog with the isopropyl radical (IX). Its structure was confirmed by the IR spectrum, in which absorption bands for a carbonyl (1709 cm^{-1}), a double bond (1620 cm^{-1}), and an ether oxygen in a tetrahydrofuran ring (1077 cm^{-1}) were found.

When the enol (XII) was heated with a 20% solution of alkali, it was broken down into ethyl propyl ketone and acetic acid. A 2,4-dinitrophenylhydrazone was obtained for the ethyl propyl ketone; it did not give any depression in melting point when mixed with a known sample.

EXPERIMENTAL

3,5-Dimethylhexyne-1-diol-3,4 (VI) (Experiment carried out by Hsü Ting-yü)

Synthesis of (I). a) By I. A. Favorskaya's method [11]. In a three-necked flask with a propeller stirrer and a reflux condenser were placed 150 g of potassium hydroxide and 500 ml of anhydrous ether. While being cooled with ice, the ether was saturated with acetylene, after which a solution of 20 g of isobutyraldehyde in 500 ml of ether was added to the flask dropwise over a period of 10 hours. The next day the reaction mixture was decomposed with 200 ml of water, the ether layer was separated off, the aqueous layer was extracted with ether, and the combined extracts were neutralized by passing a current of CO_2 through them and then dried with potassium carbonate. After removal of the ether, the residue was distilled in vacuum. The yield of methylisopropylethynylcarbinol was 20 g (73%).

B. p. 55-56° (30 mm), $n^{20}D$ 1.4359, d^{20}_4 0.8769, MR_D 29.21. $C_6H_{10}O$F. Calculated 29.43.

Literature data [11]: b.p. 51° (38 mm), $n^{20}D$ 1.4369.

b) By the method of McGrew and Adams [13]. Into a wide, thick-walled test tube, which was placed in a Dewar vessel and cooled to-(40-50°), was poured 750 ml of liquid ammonia, the mechanical stirrer was turned on, 0.05 g of $Fe(NO_3)_3 \cdot 9H_2O$ and 0.5 g of metallic sodium were added, and dry air was passed through for 3 minutes. After 15 minutes the blue color changed to gray (formation of catalyst), and then over a period of 10 minutes 23 g of sodium, cut into small pieces, was added to the liquid ammonia, after which acetylene was passed through for 1.5-2 hours. During this process, the blue color of the solution gradually disappeared and the test tube was filled with a grayish precipitate of sodium acetylide. The passage of acetylene was continued for about an hour more, after which a solution of 72 g of isobutyraldehyde in 100 ml of absolute ether was added dropwise. After evaporation of the ammonia, the residue was treated with 27 g of ammonium chloride in 250 ml of water and steam distilled; the distillate was salted out with potassium carbonate, extracted with ether, and dried with potassium carbonate. After the ether was distilled off, the residue was distilled in vacuum. B. p. 56-56.5° (30 mm). Yield 73%.

Hydration of isopropylethynylcarbinol. To a solution of 2.3 g of mercuric oxide in 125 ml of 25% sulfuric acid was added 27 g of the acetylenic alcohol (I) over a period of 2 hours with continuous stirring while the temperature was kept at 30-40°. The reaction mixture was extracted with ether, and the extracts were dried with sodium sulfate. After the ether was distilled off and the residue was distilled in vacuum, 18 g (76%) of acetylisopropylcarbinol (II) was obtained.

B. p. 74-75° (36 mm), $n^{20}D$ 1.4249, d^{20}_4 0.9453, MR_D 31.36; calculated 31.44.

Found %: C 61.16, 61.01; H 10.38, 10.61; number of active hydrogens 0.95, 1.10. $C_6H_{12}O_2$. Calculated %: C 62.07; H 10.34; number of active hydrogens 1.0.

2,4-dinitrophenylhydrazone, m.p. 142-143° (from alcohol).

Found %: N 18.90, 19.04. $C_{12}H_{16}O_4N_4$. Calculated %: N 18.95.

Synthesis of 3,5-dimethylhexyne-1-diol-3,4 (VI). a) By A. E. Favorskii's method, modified for keto alcohols by A. S. Onishchenko [3], liquid and crystalline glycol were obtained. B. p. 104-105° (20 mm). After distillation, a part of the glycol crystallized, m.p. 64-65°.

Crystalline glycol, m.p. 64-65°.

Found %: C 68.08, 68.07; H 10.00, 10.06. Number of active hydrogens 2.02, 1.94. M 141. $C_8H_{14}O_2$. Calculated %: C 67.61; H 9.90. Number of active hydrogens 2.0. M 142.

Liquid glycol, b.p. 104-105° (20 mm), $n^{20}D$ 1.4628, d^{20}_4 0.9867, MR_D 39.62. $C_8H_{14}O_2$F. Calculated 40.19.

Found %: C 66.91, 67.03; H 9.98, 10.35. Number of active hydrogens 2.08, 2.00. M 135. $C_8H_{14}O_2$. Calculated %: C 67.61; H 9.90. Number of active hydrogens 2.0. M 142.

Five-tenths of a gram of the crystalline glycol was hydrogenated in 35 ml of anhydrous alcohol in the presence of 0.1 g of platinum black. Ninety-six and one-tenth percent of the theoretical amount of hydrogen was absorbed, calculated on the basis of a triple bond. When the liquid glycol was hydrogenated, 93% of the theoretical amount of hydrogen was absorbed.

b) From the keto alcohol and sodium acetylide in liquid ammonia under the conditions described for the synthesis of the isopropylethynylcarbinol, only the liquid glycol was obtained, with the constants mentioned above. Yield 78-85%.

Reaction of 3,5-dimethylhexyne-1-diol-3,4 (VI) with sulfuric acid. a) Twenty grams of liquid glycol was boiled with stirring for 2 hours with 200 ml of 10% sulfuric acid. The ether extract from the reaction mixture was washed with sodium carbonate and with water and was dried with potassium carbonate. After the ether was distilled off, the residue was distilled at 30 mm. The following fractions were obtained: 1st, 67-100°, 2 g; 2nd, 100-104°, 2.8 g; 3rd, 108-110°, 7 g; the 2nd and 3rd fractions on repeated distillation at 30 mm yielded: 1st, 103-104°, 3 drops; 2nd, 105-107°, 9 g, $n^{20}D$ 1.4627. This fraction crystallized overnight, m.p. 64-65°.

b) Twenty grams of the glycol was heated for 4 hours with 200 ml of 20% sulfuric acid to 100°. The reaction mixture was treated as in the preceding experiment (a). On distillation at atmospheric pressure, 13 g of material was obtained.

B. p. 117-122°, $n^{20}D$ 1.4251, d^{20}_4 0.8772, MR_D 36.15 $C_8H_{12}O$F. Calculated 37.15.

2,4-Dinitrophenylhydrazone, m.p. 129-130°.

Found %: C 55.08; H 5.29; N 18.58. $C_{14}H_{16}O_4N_4$. Calculated %: C 55.26; H 5.26; N 18.42.

The ketone obtained, 3,5-dimethylhexyn-1-one-4 (VIII), gave a precipitate with an ammoniacal solution of silver oxide.

c) Eighty ml of sulfuric acid (d 1.84) was poured into a 200-ml beaker and, with stirring and cooling to -10°, 14 g of glycol was added dropwise. In 2 hours the solution came to room temperature and was poured onto 500 g of finely crushed ice. The solution obtained was saturated with ammonium sulfate and extracted with ether. After the extract was dried and the ether distilled off, the residue was distilled in vacuum at 32 mm. The following fractions were obtained: 1st, b.p. 70-93°, 2 g (15.8%); 2nd, b.p. 93-94°, 6 g (44%).

The 1st fraction gave a red precipitate with 2,4-dinitrophenylhydrazine; the derivative melted at 190-191°. A mixed sample with known 2,4-dinitrophenylhydrazone of mesityl oxide gave no depresion in melting point.

Found %: C 51.82, 51.60; H 5.20, 5.08; N 20.42, 20.25. $C_{12}H_{14}O_4N_4$. Calculated %: C 51.79; H 5.03; N 20.14.

The 2nd fraction did not react with either 2,4-dinitrophenylhydrazine or semicarbazide, was not hydrogenated in the presence of platinum black, and was not ozonized; with $FeCl_3$ solution it was colored an intense violet; it decolorized a solution of bromine in chloroform.

B. p. 93-94° (32 mm), $n^{20}D$ 1.4405, d^{20}_4 0.9328, MR_D 40.16. $C_8H_{14}O_2$F. Calculated 39.65.

Found %: C 67.79, 67.84; H 9.98, 10.00. Number of active hydrogens 0.89, 0.89. M 135. $C_8H_{14}O_2$. Calculated %: C 67.61; H 9.86. Number of active hydrogens 1. M 142.

The substance obtained was shown by analytical data and its properties to be 3-methyl-2-isopropyl-4-ketotetrahydrofuran (IX).

Reaction of 3-methyl-2-isopropyl-4-ketotetrahydrofuran with 20% potassium hydroxide solution. Five grams of the tetrahydrofuranone was distilled with a 20% solution of potassium hydroxide; the concentration of the alkali solution was kept constant by the addition to the Wurtz flask of water from a dropping funnel. The distillate was extracted with ether, the extract was dried with sodium sulfate, the ether was distilled off, and the residue was distilled. Yield 2.5 g.

B. p. 111-114°, $n^{20}D$ 1.3981, d^{20}_4 0.8014, MR_D 30.10; Calculated 29.92.

Found %: C 71.79, 71.76; H 12.20, 12.22. $C_6H_{12}O$. Calculated %: C 72.00; H 12.00.

The 2,4-dinitrophenylhydrazone melted at 107°. The structure of the ketone obtained was demonstrated by the confirmatory synthesis of ethyl isopropyl ketone, obtained by oxidation with chromic acid mixture of ethylisopropylcarbinol. The boiling point of the synthesized ketone was 114-117°, $n^{20}D$ 1.4018. The melting point of the 2,4-dinitrophenylhydrazone prepared from it was 109°. A mixed sample gave no depression in melting point.

The alkaline solution remaining after the ketone had been distilled off was acidified with sulfuric acid, the volatile acid was steam-distilled off and the silver salt, which corresponded to acetic acid, was prepared.

Found %: Ag 64.50, 64.40, $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

3-Methylheptyne-1-diol-3,4 (XI). (Experiment carried out by L. N. Il'ina)

Synthesis of n-propylethynylcarbinol (III). a) By the method of I. A. Favorskaya [11]. From 25 g of butyraldehyde, 16-19 g of the alcohol (47-55%) was obtained by this method. B. p. 42-43° (8 mm).

b) By the method of McGrew and Adams [13] in liquid ammonia medium. From 36 g of butyraldehyde, 15 g (30%) of propylethynylcarbinol was obtained.

B. p. 52-53° (12 mm), $n^{20}D$ 1.4340, d^{20}_4 0.8714, MR_D 29.26. $C_6H_{10}O$. Calculated 29.43.

Literature data [11]: b.p. 87-88° (100 mm), $n^{20}D$ 1.4350, d^{20}_4 0.8710; b.p. 140-141°, $n^{20}D$ 1.4390, d^{20}_4 0.8704.

Hydration of n-propylethynylcarbinol (III). Four and two-tenths grams of mercuric oxide was dissolved in 25 ml of concentrated sulfuric acid and poured into 150 ml of water. After the solution was cooled to room temperature, 50 g of propylethynylcarbinol was added with vigorous stirring. Stirring was continued for 2.5 hours. At the end of the reaction the upper oily layer was separated off and an ether extract was made from the aqueous layer, the extract was dried with sodium sulfate, and the ether was distilled off and the residue distilled in vacuum. The first fraction was n-propylacetylcarbinol (IV), b.p. 58-60° (9 mm), 15-20 g (30%); 2nd fraction, b.p. 124-126° (13 mm); 30%.

Propylacetylcarbinol. B. p. 58-60° (9 mm), $n^{20}D$ 1.4266, d^{20}_4 0.9566, MR_D 31.11; calculated 31.44.

Literature [16]: b.p. 163-165°.

Found %: C 61.70, 61.88, H 10.33, 10.34. M 119. $C_6H_{12}O_2$. Calculated %: C 62.07; H 10.35. M 116.

The 2,4-dinitrophenylhydrazone of propylacetylcarbinol melted at 102-103°.

Found %: N 19.21. $C_{12}H_{16}O_5N_4$. Calculated %: N 18.92.

The 2nd fraction decolorized potassium permanganate solution, contained neither a hydroxyl nor a carbonyl group, and did not react with ammoniacal silver oxide solution.

B.p. 124-126° (13 mm), $n^{20}D$ 1.4740, d^{20}_4 0.9585, MR_D 57.47. $C_{12}H_{20}O_2F_2$. Calculated 57.78.

Found %: C* 72.13, 72.24. H 10.08, 10.28. M 190. $C_{12}H_{20}O_2$. Calculated %: C 73.47; H 10.20. M 196.

Compound (V) can be considered to be 2,6-dimethyl-3,5-dipropyldioxadiene-1,4.

When 10 g of this compound was oxidized, 24.5 g of potassium permanganate was used up; theoretical 21.5 g. Neutral products were not isolated. Of the acids it was possible to isolate only acetic acid, b.p. 115-119°.

Found %: Ag 64.55, 64.07. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

In order to decrease the yield of byproduct (V) in the synthesis of n-propylacetylcarbonyl by the method of Kucherov, the propylethynylcarbinol added was diluted with ether, and in this case the propylacetylcarbinol was the sole reaction product.

Synthesis of 3-methylheptyne-1-diol-3,4 (XI). The glycol was prepared from n-propylacetylcarbinol and sodium acetylide in liquid ammonia, under the conditions described above, in 30-35% yield. The 3-methylheptyne-1-diol-3,4 was a thick yellowish liquid, which quickly turned dark in the air.

B. p. 87-89° (4 mm), 110-111° (18 mm), $n^{20}D$ 1.4609, d^{20}_4 0.9743, MR_D 40.33. $C_8H_{14}O_2F$. Calculated 40.19.

Found %: C 66.26, 66.18; H 10.13, 9.94. M 139. $C_8H_{14}O_2$. Calculated %: C 67.61; H 9.86. M 142.

*In spite of the fact that the product was carefully purified several times by distillation, the analyses for carbon proved to be low.

Reaction of 3-methylheptyne-1-diol-3,4 with sulfuric acid (XI). The reaction was carried out under the conditions of Onishchenko [5], as described above for 3,5-dimethylhexyne-1-diol-3,4. Five grams of reaction product, 4 g of tar, and 0.5 g of a low-boiling fraction were obtained from 10 g of the glycol.

B.p. 74-76° (11 mm), $n^{20}D$ 1.4420, d^{20}_4 0.9330, MR_D 45.04. $C_8H_{14}O_2F$. Calculated 39.65.

Found %: C 67.33, 67.39; H 9.91, 9.95; OH 11.41, 11.03. M 142. $C_8H_{14}O_2$. Calculated %: C 67.61; H 9.86; OH 11.96. M 142.

The compound (XII) obtained was 3-methyl-2-propyl-4-ketotetrahydrofuran.

The compound decolorized a solution of potassium permanganate, but when it was hydrogenated over platinum catalyst, addition of hydrogen was not observed. The compound did not give a precipitate with 2,4-dinitrophenylhydrazine, but was colored intense violet by the action of an alcoholic solution of ferric chloride.

Reaction of 3-methyl-2-propyl-4-hydroxydihydrofuran-2,5 (XII) with 20% potassium hydroxide solution. Five grams of the compound was distilled with 25 ml of 20% potassium hydroxide solution. In order to keep the concentration of alkali unchanged, water was added continuously from a dropping funnel. The distillate was extracted with ether and the extract dried with sodium sulfate. The ether was distilled off and the residue was distilled at 123-124°, $n^{20}D$ 1.4015. Literature data [17]: b.p. 123-123.5°, $n^{20}D$ 1.3990.

The 2,4-dinitrophenylhydrazone melted at 127-128° (from alcohol). A mixed sample with the 2,4-dinitrophenylhydrazone prepared by confirmatory synthesis by oxidation of ethylpropylcarbinol with chromic acid mixture gave no depression in melting point.

The alkaline solution after the distillation of the ethyl propyl ketone was acidified with sulfuric acid and the volatile acid was steam distilled off. The silver salt of acetic acid was obtained from the distillate.

Found %: Ag 64.29, 64.18. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

SUMMARY

1. The secondary-tertiary acetylenic α-glycols 3,5-dimethylhexyne-1-diol-3,4 and 3-methylheptyne-1-diol-3,4 were synthesized by the condensation of the appropriate keto alcohols with sodium acetylide in liquid ammonia and the reaction of these glycols with sulfuric acid was studied.

2. It was shown that when 3,5-dimethylhexyne-1-diol-3,4 is heated with 20% sulfuric acid, it undergoes a pinacoline rearrangement with the formation of an acetylenic ketone, 3,5-dimethylhexyn-1-one-4. When the two glycols react with concentrated sulfuric acid at -10°, both of them are converted into a mixture of 3-methyl-2-isopropyl-(or n-propyl)-4-ketotetrahydrofuran-2,5 and the corresponding enols. 3,5-Dimethylhexyne-1-diol-3,4 under these conditions, furthermore, is partially decomposed with the formation of mesityl oxide.

3. A possible mechanism has been proposed for the conversions studied.

4. The hydrolytic cleavage in alkaline medium of the cyclic compounds obtained was studied and it was shown that in this process the formation of ethyl isopropyl and ethyl propyl ketones and ketene, which is converted under the reaction conditions to acetic acid, takes place.

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CONDENSATION OF 3,3-DIMETHYL-1-PHENYL-1-HYDROXYPHTHALAN AND 5,5-DIMETHYL-2,4-DIPHENYL-2-HYDROXYDIHYDROFURAN-2,5 WITH ACETIC ANHYDRIDE

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It has been shown in previous communications that hydroxydihydrofurans and hydroxyphthalans have similar properties and also exhibit a similarity to xanthydrol and triarylcarbinols [1-3]. In particular, all of the compounds mentioned are comparatively easily condensed with compounds containing labile hydrogen atoms in the methyl and methylene groups. Numerous condensations of xanthydrol with malonic and cyanoacetic esters, anhydrides of aliphatic acids [4], various phenols [5], amines of the aromatic series [6], and other compounds have been described. Condensations of triarylcarbinols also are well known (see, for example, [7]).

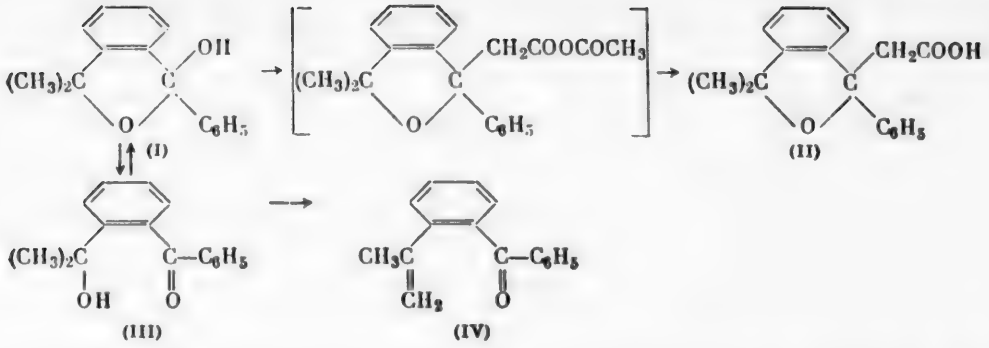
The ability of hydroxyphthalans to condense had been shown prior to our work through the example of 1,3,3-triphenyl-1-hydroxyphthalan. Reaction products were obtained from it with phenol and dimethylaniline [8].

In studying the properties of the hydroxydihydrofurans and hydroxyphthalans, we carried out condensation reactions of 5,5,-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 with phenylmethylpyrazolone [9] and acetone [2], and of 3,3-dimethyl-1-(p-tolyl)-and 3,3-dimethyl-1-(p-anisyl)-1-hydroxyphthalans with phenylmethylpyrazolone [3].

Continuing our experiments on condensation, we investigated the effect of acetic anhydride on 3,3-dimethyl-1-phenyl-1-hydroxyphthalan (I), which was first prepared in 1927 [10] and was investigated in detail by A. Fabritsy [11]. Among other reactions, A. Fabritsy carried out the condensation of this hydroxyphthalan with dimethylaniline.

When a solution of hydroxyphthalan was boiled in acetic anhydride for 2 hours, a small amount of solid material was obtained, which had acid properties. It was found that the yield of the acid increased upon more prolonged boiling and the addition of several drops of piperidine. The yield of acid also increased when a small amount of perchloric acid was added, but in this case the reaction mixture resinified and it was difficult to purify the product. According to analytical data obtained, the compound was a condensation product of hydroxyphthalan (I) and acetic acid. It contained one active hydrogen atom, was extraordinarily stable toward oxidizing agents, did not decolorize bromine, and gave no reaction for a carbinol group. On the basis of the data obtained, it was possible to ascribe to the compound that was formed the structure of 3,3-dimethyl-1-phenylphthalyl-1-acetic acid (II).

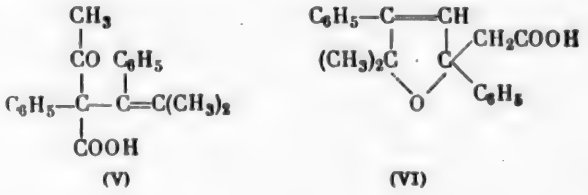
Besides the acid product, in all the condensation experiments a thick oil was formed, which solidified after distillation in vacuum and was identified as o-isopropenylbenzophenone (IV), previously obtained by distillation of 3,3-dimethyl-1-phenyl-1-hydroxyphthalan (I) at atmospheric pressure [10].



(I) (II) (III) (IV)

It had been shown previously that hydroxyphthalans can react in ring (I) and open (III) forms [3, 10, 12]. o-Isopropenylbenzophenone was formed as a result of the dehydration of the open, hydroxyketone form of 3,3-dimethyl-1-phenyl-1-hydroxyphthalan.

The results obtained cast doubt on the structure previously suggested for the acid with m.p. 137-138° which was formed by the action of acetic anhydride on 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 [13, 14] and gave rise to the suggestion that this compound was not phenyl-(1-phenylisocrotyl)acetoacetic acid (V) but 5,5-dimethyl-2,4-diphenyl-2,5-dihydrofuryl-2-acetic acid (VI).



(V) (VI)

Actually, if the acid under consideration corresponded to structure (V) and if it were formed by the previously shown mechanism [14], then a similar reaction should take place with benzoic anhydride, but we were unable to bring about the reaction of the hydroxydihydrofuran with benzoic anhydride.

On the other hand, 3,3-dimethyl-1-phenyl-1-hydroxyphthalan, which is similar in all its properties to the hydroxydihydrofuran, could not react with acetic anhydride by the previously proposed scheme [14], since isomerization of the corresponding acetate to the substituted acetyl derivative is impossible because of the absence in the dihydrofuran ring of the hydroxyphthalan of a hydrogen atom in position 3.

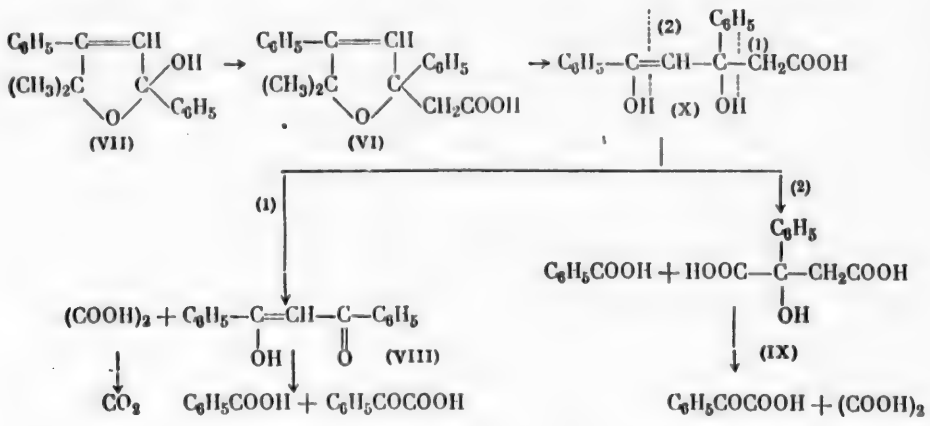
To confirm the proposed structure for acid (VI), which was obtained by the reaction of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (VII) with acetic anhydride, we carried out several experiments on the oxidation of this acid with potassium permanganate in alkaline medium, using a larger amount of the starting acid than before [14], modifying the reaction conditions somewhat, and investigating the intermediate oxidation products with especial care.

It was found that the neutral products of the oxidation were acetone and dibenzoylmethane (VIII), the latter of which was previously taken [14] to be phenylacetylbenzoylmethane, which had not been described in the literature. The carbon content of these β-diketones is very close, as well as the nitrogen content of the corresponding pyrazoles.• In one of the experiments a slight amount of acetophenone was detected, the formation of which could be explained by the alkaline decomposition of dibenzoylmethane [15].

From the acid oxidation products we isolated α-phenyl-α-hydroxysuccinic (α-phenylmalic) acid (IX) [16] and oxalic acid with an admixture of benzoic and benzoylformic acids—products of the further oxidation of dibenzoylmethane and α-phenylmalic acid—and also sometimes carbon dioxide gas, which was obtained as a result of the oxidation of oxalic acid.

•Unfortunately, the percentage of carbon and hydrogen in the pyrazole obtained was not determined because of the small quantity of this compound.

The compound obtained from the oxidation of the acid with m.p. 137-138° confirmed the structure proposed for it—5,5-dimethyl-2,4-diphenyl-2,5-dihydrofuryl-2-acetic acid (VI)—and its oxidation can be represented by the following diagram.



The first oxidation product, the hydroxyketo acid (X), could not be isolated, and it apparently was oxidized very rapidly by the two routes (1) and (2) with the formation of dibenzoylmethane (VIII) and oxalic acid• (1) and of α-phenylmalic acid (IX) and benzoic acid (2). In all the oxidation experiments carried out we found the β-diketone (VIII), which was the main product under the conditions of alkaline oxidation used by us. α-Phenylmalic acid was very difficult to isolate because of the possibility of its dehydration and further oxidation to benzoylformic and oxalic acids.

It was noted that in all the experiments on oxidation a considerable amount of the starting acid (40-45%) was recovered, which greatly hindered the isolation of the oxidation products in the pure form. An excess of oxidizing agent, however, did not increase the yields of the diketone and the α-phenylmalic acid, since these compounds are oxidized much more easily than the starting acid. The addition of alkali at the time of the reaction greatly accelerated the oxidation process, decreased the recovery of the starting material, and increased the yield of the diketone (VIII).

When the maximum yields of dibenzoylmethane (39%) and α-phenylmalic acid (10.7%) were compared, it was seen that the oxidation of 5,5-dimethyl-2,4-diphenyl-2,5-dihydrofuryl-2-acetic acid (VI) goes primarily in the direction of (1) (see diagram), i.e., in this case the double bond in the dihydrofuran ring of the starting acid is very stable, as we found previously in the oxidation of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 [17].

The product of the reaction of 5-methyl-2,4,5-triphenyl-2-hydroxydihydrofuran-2,5 with acetic anhydride, which we described in [18], according to the ideas that we advanced also should correspond to the substituted acetic acid 5-methyl-2,4,5-triphenyldihydrofuryl-2-acetic acid, and not to the substituted unsaturated β-keto acid 2,3,4-triphenyl-2-acetylpentene-3-carboxylic acid, for which it previously was taken [18]. The results of the oxidation of this acid do not contradict this statement.

EXPERIMENTAL

Action of Acetic Anhydride on 3,3-Dimethyl-1-phenyl-1-hydroxyphthalan

3,3-Dimethyl-1-phenyl-1-hydroxyphthalan was prepared from dimethylphthalide and phenylmagnesium bromide [10].

To a solution of 6 g of the hydroxyphthalan in 36 ml of acetic anhydride was added 10 drops of piperidine, and the solution was heated to boiling for 4 hours, after which the reaction mixture was poured into water. The

•In the first oxidation [14] we did not look for oxalic acid.

next day the oily residue was dissolved in ether and the ether solution was washed with 1.0 N sodium hydroxide solution and dried with calcined sodium sulfate.

The alkaline solution was acidified, treated with ether, the ether extract was dried, and the ether was distilled off. After removal of the ether, a solid material was obtained, which did not decolorize bromine, reacted with methylmagnesium iodide, and dissolved in bicarbonate solution, where upon acidification of the solution the material was separated unchanged.

The acid obtained was soluble in alcohol, ether, and benzene, insoluble in water and petroleum ether.

Two and five-tenths grams (35.5%) of a compound with m.p. 106-107° (ether + petroleum ether) was obtained.

Found %: C 76.65, 76.68; H 6.58, 6.65. M 287. Number of active hydrogens 0.96. Acid equiv. 274. $C_{18}H_{18}O_3$. Calculated %: C 76.58; H 6.42. M 282.3. Number of active hydrogens 1. Acid equiv. 282.3.

Thus, according to the properties and the analytical data we can ascribe to the compound the structure of 3,3-dimethyl-1-phenylphthalyl-1-acetic acid.

Silver salt. Five-tenths of a gram of the acid was converted to the ammonium salt, which was dissolved in the minimum amount of water, and a solution of silver nitrate was added to the aqueous solution. The precipitate of silver salt was filtered off, washed with a small amount of ether, and dried at 50° in a thermostat, then in a desiccator. The salt darkened on standing.

Found %: C 56.08, 56.15; H 4.66, 4.65; Ag 27.76, 27.52. $C_{18}H_{17}O_3Ag$. Calculated %: C 55.55; H 4.40; Ag 27.72.

Amide. Five-tenths of a gram of the acid was heated with 3 ml of thionyl chloride to gentle boiling for 40 minutes. The excess thionyl chloride was distilled off, leaving a thick brownish liquid that was poured into a cooled concentrated ammonia solution. Five-tenths of a gram of grayish precipitate separated out. The compound was recrystallized twice from aqueous alcohol. M.p. 144-145°.

Found %: C 76.44, 76.54; H 7.13, 7.03; N 4.99, 4.81. $C_{18}H_{19}O_2N$. Calculated %: C 76.76; H 6.92; N 4.97.

After the ether was distilled off from the extract, which had been washed with alkali, 3.3 g of a light yellow, thick oil was obtained, which did not crystallize upon long standing. The compound did not contain active hydrogen and it easily decolorized potassium permanganate solution and bromine water.

After being distilled twice in vacuum at 149-151° (2 mm) the oil solidified. Needle-shaped crystals were obtained with m.p. 42-43° (from aqueous alcohol). M.p. 44° is given for o-isopropenylbenzophenone [10]. Yield 2.9 g (52.4%).

By treatment with an alcoholic solution of 2,4-dinitrophenylhydrazine containing a small amount of hydrochloric acid [19], an orange 2,4-dinitrophenylhydrazone was obtained with m.p. 199-200° (from glacial acetic acid).

Found %: C 65.67, 65.65; H 4.73, 4.80; N 14.03, 14.06. $C_{22}H_{18}O_4N_4$. Calculated %: C 65.65, H 4.51; N 13.92.

Action of Acetic Anhydride on 5,5-Dimethyl-2,4-diphenyl-2-hydroxydihydrofuran 2,5

To determine the structure of the acid with m.p. 137-138° obtained by the action of acetic anhydride on the hydroxydihydrofuran [13, 14], six experiments were carried out on the oxidation of this acid by potassium permanganate.

We shall cite two experiments: In one the main attention was given to the isolation and study of the acid oxidation products, and in the other to the neutral products.

Experiment 1. For 10 g of the acid, 18 g of potassium permanganate was used (5 active oxygen atoms per molecule of acid). With vigorous stirring at room temperature, 500 ml of 2% potassium permanganate solution containing 3.5 g of potassium hydroxide was added to the acid over a period of 1.5 hours. A slight warming of the reaction mixture was observed, and therefore the temperature of the reaction was regulated by the rate of

addition of the oxidizing agent. The remainder of the dry oxidizing agent (8 g) was added in 6 lots over 2 hours with subsequent stirring for 3 hours. In a day the clear solution was filtered off from the manganese dioxide, from which about 0.3 g of acetophenone was extracted after a washing with ether; 2,4-dinitrophenylhydrazone m.p. 245-247° (mixed m.p.). When a small portion of the filtrate was distilled off, acetone was detected; 2,4-dinitrophenylhydrazone m.p. 126° (mixed m.p.).

From the remaining portion of the filtrate an ether extract was made, which yielded a total of 0.6 g of a thick oily material that solidified rather quickly in the air and had an unsharp m.p. 72-77°. The compound gave a reaction for an enol and reacted with p-nitrophenylhydrazine to form a bright orange precipitate with m.p. 136-137°. A similar compound was obtained by us earlier also [14]; it was investigated in detail in Expt. 2.

Upon careful decomposition of the salts of the organic acids with dilute sulfuric acid, benzoic acid first separated out in the form of a light scum (m.p. 120°, mixed m.p.). On further acidification and stirring, the amount of insoluble acids increased, but all were churned together in a sticky grayish-yellow lump, which could be separated from the clear solution. In the solution was found benzoylformic acid, dinitrophenylhydrazone m.p. 195-196° (mixed m.p.) [20], and after it had been extracted once with ether, prolonged extraction of the remaining liquid yielded oxalic acid, which was characterized by its melting point (101°) and its calcium salt.

Found %: Ca 31.16, 31.08. C_2O_4Ca. Calculated %: Ca 31.25.

The sticky grayish-yellow lump which was separated upon acidification of the salts of the organic acids was washed with water and dissolved in ether. The ether solution, which showed a reaction for an enol, was carefully washed several times with an aqueous solution of sodium carbonate to separate the acids from the enol (the enol is insoluble in sodium carbonate), which apparently was mixed with the salts of the organic acids in the form of the enolate and was separated along with the acids upon acidification. After removal of the ether, 1.7 g of neutral crystalline material remained with m.p. 78-79°, corresponding to dibenzoylmethane [15], which was investigated in detail in Expt. 2. The total yield of dibenzoylmethane, taking into account 0.6 g that was isolated from the neutral oxidation products, was 2.3 g (31% based on the full amount of the starting acid and 52.3% based on that which entered into the reaction).

The alkaline solution of the salts after removal of the enol, upon decomposition with sulfuric acid again yielded a grayish lump, but of a firmer consistency, which after washing with water and drying in the air was converted to a brittle grayish mass (7.3 g) that melted within the range 52-74°. From 6 g of this mass we obtained by repeated recrystallization from alcohol, and ether mixed with petroleum ether, 4 g (40%) of the starting acid with m.p. 135-136.5° (mixed m.p.) and 0.73 g of α-phenylmalic acid [16, 21] with m.p. 185-186°, more easily soluble in organic solvents than the starting acid. The yield of α-phenylmalic acid was 10.7%, based on the starting acid taken for the reaction and 18% based on the amount that actually reacted.

Found %: C 57.42, 57.35; H 4.97, 4.83. M 201.5. $C_{10}H_{10}O_5$. Calculated %: C 57.14; H 4.76. M 210.•

The remaining portion of the brittle grayish mass, which was mainly a mixture of the starting 5,5-dimethyl-2,4-diphenyldihydrofuryl-2-acetic acid with α-phenylmalic acid, with the former predominating, was boiled several times with water and the hot aqueous solution was poured off from the insoluble part. After the clear aqueous solution cooled, it became turbid. A very small amount of clear, rather large crystals with m.p. 160-162° was extracted with ether, and these gave a depression in melting point with all the acids previously isolated from the oxidation. The crystals were rather easily soluble in water, particularly in hot water, showed a sharp acid reaction, and immediately decolorized an aqueous solution of potassium permanganate and bromine solution. Apparently this was a product of the dehydration of α-phenylmalic acid, possibly phenylfumaric acid, for which the m.p. 161° was given in the earlier literature [22]. However, in later investigations [23, 24] the m.p. 128-129° was given for phenylfumaric acid. We could not establish the nature of the acid with 128-129° obtained by us because of the small amount of it, and also it did not enter into our problem; therefore we could not confirm that this acid was phenylfumaric. However, this acid corresponds to a compound obtained previously on recrystallization of α-phenylmalic acid from hot water [22].

•We were unable to determine the active hydrogen of the acid, since a complex very difficultly soluble in ether was formed with Grignard reagent and therefore low results were obtained.

Experiment 2. To 7.7 g of the acid (m.p. 137-138°) was added a 2% solution of 12 g of potassium permanganate over a period of 30 minutes, with vigorous stirring. No external signs of oxidation were observed, and therefore we added a solution of 1.3 g of potassium hydroxide over a period of 30 minutes. Decolorization began immediately with considerable evolution of heat, so that it was necessary to resort to external cooling. After an hour, 1.8 g of the oxidizing agent was added to the reaction mixture in small portions (total amount of $KMnO_4$ 13.8 g, i.e., as in Expt. 1, 5 active oxygen atoms to 1 molecule of starting material). The whole reaction lasted 3.5 hours. Afterwards, a strong current of carbon dioxide gas was passed through the mixture to tie up any free alkali and displace the enol from the enolate. After 10 hours, the manganese dioxide was filtered off, washed with small amounts of hot water and several times with small portions of ether. From the ether we obtained 1.2 g of the starting acid with m.p. 135-136.5° (mixed m.p.). The neutral products volatile with steam were distilled off from the filtrate under slight vacuum and with heating on a water bath (65-75°). In the first fractions of distillate we detected acetone in the form of the 2,4-dinitrophenylhydrazone (mixed m.p.), and from the last fractions we extracted with ether a thick light yellow substance that crystallized rather quickly upon standing. After being dried on a porous plate, this material melted at 78-79°. It was soluble in the usual organic solvents and in solutions of alkalies, and gave a reaction for enol with ferric chloride [15]. Yield 2.2 g (39% based on the starting acid and 71% based on the acid reacting).

Found %: C 80.38; H 5.64. M 222. $C_{15}H_{12}O_2$. Calculated %: C 80.36; H 5.33. M 224.

With p-nitrophenylhydrazine the compound gave 3,5-diphenyl-1-(p-nitrophenyl)pyrazole with m.p. 137-138°.

Found %: C 73.60; H 4.51; N 12.10, 12.22. $C_{21}H_{15}O_2N_3$. Calculated %: C 73.83; H 4.39; N 12.31.

With semicarbazide hydrochloride and potassium acetate we obtained the amide of 3,5-diphenyl-1-pyrazolecarboxylic acid with m.p. 201-203° [25].

Found %: C 72.77; H 5.16; N 16.14, 16.22. $C_{16}H_{13}ON_3$. Calculated %: C 73.00; H 4.94, N 15.97.

When the salts of the organic acids were neutralized, as in Expt. 1, a grayish-yellow lump was produced, but more compact, from which 2.3 g of the starting acid (mixed m.p.) was isolated by prolonged recrystallization. The yield of acid that did not enter into the reaction was 45%, taking into account 1.2 g of the acid that was obtained on washing the manganese dioxide. The yield of α-phenylmalic acid with m.p. 184.5-186° (mixed sample with acid obtained in Expt. 1) was 0.4 g (19% based on the starting acid and 89% based on the acid that reacted). The oxalic acid, contaminated with a small amount of benzoylformic acid, was recovered from the extracts from the solution after removal of the water-insoluble acids.

SUMMARY

1. When acetic anhydride acts on 3,3-dimethyl-1-phenyl-1-hydroxyphthalan, a condensation product is formed—3,3-dimethyl-1-phenylphthalyl-1-acetic acid. At the same time dehydration of the starting hydroxyphthalan takes place with the formation of o-isopropenylbenzophenone.

2. It has been shown that when acetic anhydride reacts with 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5, a similar condensation product is formed—5,5-dimethyl-2,4-diphenyldihydrofuryl-2-acetic acid, the structure of which was confirmed by obtaining from its oxidation dibenzoylmethane and α-phenylmalic acid.

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SYNTHETIC ANESTHETIC SUBSTANCES

ESTERS OF STEREOISOMERIC 1,2,5-TRIMETHYL-4-ETHYNYL-, 1,2,5-TRIMETHYL-4-ETHYL-, AND 1,2,5-TRIMETHYL-4-ACETYL-4-PIPERIDOLS

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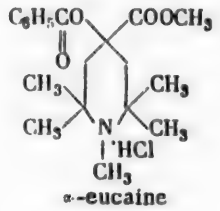
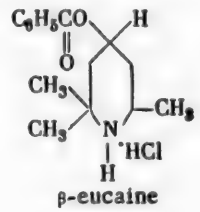
One of the most powerful anesthetics is dicaine (hydrochloride of the β-dimethylaminoethyl ester of p-butylaminobenzoic acid), which is employed for infiltration and cerebrospinal anesthesia and has a more prolonged effect than novocaine in concentrations 5-10 times lower. In recent years the utilization of dicaine in surgical practice has been greatly reduced due to its high toxicity and to the grave consequences sometimes resulting from cerebrospinal anesthesia.

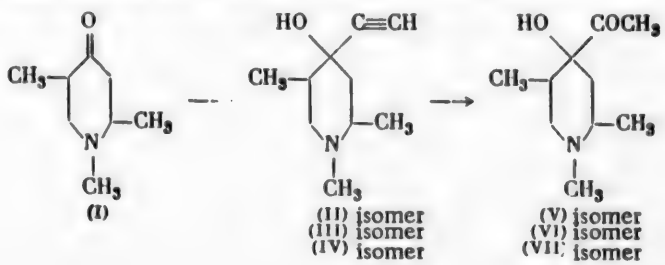
Recently we undertook an investigation of esters of various 4-piperidols with the objectives of synthesizing new anesthetics, establishing their pharmacological value and determining the relation between anesthetizing activity and chemical structure. Judging by pharmacological tests, some preparations of this class [1] have an activity close to that of dicaine in radical and infiltration anesthesia while being 4-8 times less toxic.

In the present paper we describe esters of stereoisomeric 1,2,5-trimethyl-4-ethynyl-, 1,2,5-trimethyl-4-ethyl-, and 1,2,5-trimethyl-4-acetyl-4-piperidols; these constitute the piperidinic fragments of alkaloids of the tropane series (cocaine and tropacocaine) and modified analogs of known synthetic anesthetics— α- and β-eucaines [2, 3].


α-eucaine


β-eucaine

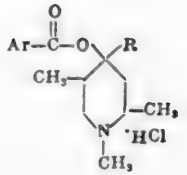
The starting substances for these preparations—stereoisomeric piperidinic acetylenic alcohols (II-IV) and ketones (V-VII)—have been described in the preceding communications [4, 5]; they are now readily accessible compounds. Their synthesis is based on the commercially available 1,2,5-trimethyl-4-piperidone (I) [6].


(I)

(II) isomer
(III) isomer
(IV) isomer

(V) isomer
(VI) isomer
(VII) isomer

Esters of 1,2,5-Trimethyl-4-ethynyl-, 1,2,5-Trimethyl-4-ethyl-, and 1,2,5-Trimethyl-4-acetyl-4-piperidols



No. of compound	R	Ar	Isomer	Melting point	Solvent for recrystallization	Yield (%)	Empirical formula	% N found	% N calculated
(VIII)	CH≡C	C_6H_5	γ	218—219	alc•	65	$C_{17}H_{22}O_2NCl$	4.36	4.54
(IX)	CH≡C	$C_6H_5CH_2$	β	208—209	alc + ac	59.3	$C_{18}H_{24}O_2NCl$	4.02	4.35
(X)	CH≡C	$C_6H_5CH_2$	γ	199—200	alc	40	$C_{18}H_{24}O_2NCl$	4.70	4.35
(XI)	CH≡C	$C_6H_5OCH_2$	γ	210—211	alc	60	$C_{18}H_{24}O_3NCl$	4.18	4.10
(XII)	CH≡C	C_6H_5CH=CH	β	208—209	alc	67.5	$C_{19}H_{24}O_2NCl$	4.28	4.20
(XIII)	CH≡C	C_6H_5CH=CH	γ	205—207	alc	72	$C_{19}H_{24}O_2NCl$	4.25	4.20
XIV)	CH≡C	$C_6H_5CH_2CH_2$	γ	143—144	alc	40	$C_{19}H_{26}O_2NCl$	4.33	4.17
(XV)	CH≡C	p-$NO_2C_6H_4$	β	202—203	alc	50	$C_{17}H_{21}O_4N_2Cl$	7.89	7.95
(XVI)	CH≡C	p-$NO_2C_6H_4$	γ	214—215	alc	52	$C_{17}H_{21}O_4N_2Cl$	7.89	7.95
(XVII)	C_2H_5	$C_6H_5CH_2CH_2$	β	112—113	ac	77	$C_{19}H_{30}O_2NCl$	3.91	4.09
(XVIII)	C_2H_5	$C_6H_5CH_2CH_2$	γ	134—135	ac	68	$C_{19}H_{30}O_2NCl$	4.15	4.09
(XIX)	C_2H_5	p-$NH_2C_6H_4$	β	141.5—143	ac	63.1	$C_{17}H_{27}O_2N_2Cl$	8.72	8.56
(XX)	C_2H_5	p-$NH_2C_6H_4$	γ	122—123	ac	75.1	$C_{17}H_{27}O_2N_2Cl$	8.68	8.56
(XXI)••	CH_3CO	CH_3	β	55—56	l	88	$C_{12}H_{21}O_3N$	6.33	6.16
(XXII)••	CH_3CO	CH_3	γ	B. p. 124—125(6mm)	—	64	$C_{12}H_{21}O_3N$	6.18	6.16
(XXIII)	CH_3CO	$C_6H_5OCH_2$	β	177—179	alc	30	$C_{18}H_{26}O_4NCl$	4.20	3.94
(XXIV)	CH_3CO	$C_6H_5OCH_2$	γ	180—181	ac	56	$C_{18}H_{26}O_4NCl$	4.23	3.94
(XXV)	CH_3CO	C_6H_5CH=CH	β	160—161	ac	98	$C_{19}H_{26}O_3NCl$	3.74	3.98
(XXVI)	CH_3CO	C_6H_5CH=CH	γ	229—230	alc	95.5	$C_{19}H_{26}O_3NCl$	3.85	3.98
(XXVII)	CH_3CO	p-$NO_2C_6H_4$	β	205—206	alc + ac	80.2	$C_{17}H_{23}O_5N_2Cl$	7.71	7.54
(XXXIII)	CH_3CO	p-$NO_2C_6H_4$	γ	221—222	alc	95	$C_{17}H_{23}O_5N_2Cl$	7.75	7.54
(XVIX)	CH_3CO	$C_6H_5CH_2CH_2$	β	145—147	ac	83	$C_{19}H_{28}O_3NCl$	4.28	3.96
(XXX)	CH_3CO	$C_6H_5CH_2CH_2$	γ	87—89	ac	84	$C_{19}H_{28}O_3NCl$	4.23	3.96
(XXXI)	CH_3CO	p-$NH_2C_6H_4$	β	132—133	ac	84.5	$C_{17}H_{27}O_3N_2Cl$	8.08	8.23
(XXXII)	CH_3CO	p-$NH_2C_6H_4$	γ	184—185	alc	79.5	$C_{17}H_{25}O_3N_2Cl$	8.40	8.23

•alc = alcohol, ac = acetone, l = ligroin.

••Esters isolated in the form of the bases.

Of the four theoretically possible stereoisomeric acetylenic alcohols (and in turn of the ketols), the synthetic process yields only three, with marked predominance of two of them (the β- and γ-isomers). The ratios between these isomers can be easily varied by altering the experimental conditions—in particular the excess acetylene pressure [4]. The synthesis can therefore be steered in the direction of predominance of the β- or γ-isomer, while the proportion of the third (the α-isomer) only changes to a minor extent.

Some acyl derivatives of β- and γ-isomers of acetylenic alcohols and of the corresponding ketols (acetates, propionates and benzoates) were previously described [5, 7], and it was found that the benzoates surpass cocaine in anesthetizing activity and are 3-5 times more active than novocaine.

Interest was now attached to the study in this series of esters of other aromatic and fatty-aromatic acids whose anesthetizing activity is usually considerably superior to that of benzoates.

The starting substances selected for preparation of new anesthetics were the most readily accessible β- and γ-isomers of acetylenic alcohols (III) and (IV) and the corresponding ketoalcohols (VI) and (VII). This series permits a broad study of the relation between anesthetizing activity of the preparations and the nature of the acylating acid on the one hand, and the spatial configuration of the starting compounds, on the other hand.

The stereoisomeric esters (VIII-XVI) were synthesized by interaction of the bases of the β- and γ-isomers of the acetylenic alcohols with a 20-30% excess of the acid chlorides at 120-170° for 1.5-2 hr. This step was usually followed by isolation of the crystalline hydrochlorides needed for pharmacological tests.

It was noted that the γ-isomer of the acetylenic alcohol enters into reaction much more easily than the β-isomer and is esterified even at 120-130°. The very much lower-melting β-isomer of the acetylenic alcohol requires higher temperatures for acylation (150-170°). Slight deviations from the standard conditions were necessitated for preparation of the benzoate (VIII) and phenoxyacetate (XI). Synthesis of the phenoxyacetate and β-phenylpropionate of the β-isomer of the acetylenic alcohol could not be realized by any of the known methods.

Hydrogenation of the stereoisomeric cinnamic esters (XII) and (XIII) and of the p-nitrobenzoates (XV) and (XVI) readily led to the corresponding β-phenylpropionates (XVII) and (XVIII) and p-aminobenzoates (XIX) and (XX) of the stereoisomeric 1,2,5-trimethyl-4-ethyl-4-piperidols, which are likewise pharmacologically interesting.

The stereoisomeric esters (XXIII-XXVIII) were synthesized by heating the bases of the ketoalcohols (XVI) and (VII) with excess of the appropriate acid chloride in benzene for 5-6 hr on a boiling water bath. The stereoisomeric β-phenylpropionates (XXIX) and (XXX) and the p-aminobenzoates (XXXI) and (XXXII) were prepared by hydrogenation in presence of Raney nickel of the corresponding stereoisomeric cinnamic esters (XXV) and (XXVI) and p-nitrobenzoates (XXVII) and (XXVIII).

In addition to the above esters, syntheses were also effected of the stereoisomeric acetates (XXI) and (XXII) needed as intermediates for investigation of synthetic routes to new analgesics of the ketobemidon type [8].

Yields, constants and analyses of the synthesized compounds are set forth in the table.

EXPERIMENTAL*

Benzoate of 1,2,5-trimethyl-4-ethynyl-4-piperidol (γ-isomer) (VIII). A mixture of 6.7 g of the hydrochloride of the γ-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol (m.p. 209-210°) [4], 25 ml of dry pyridine, and 6 g of freshly distilled benzoyl chloride was heated for 3 hr at 120-130°; the pyridine was removed in vacuo; the residue was pulverized under anhydrous ether, filtered and dried in a vacuum desiccator. Recrystallization gave 5.1 g of the hydrochloride of the benzoate.

Phenylacetate of 1,2,5-trimethyl-4-ethynyl-4-piperidol (γ-isomer) (X). A mixture of 4 g of the γ-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol (m.p. 177-178°) and 4.45 g of phenylacetyl chloride was heated for 1.5 hr at 130-135°. The reaction product was dissolved in 30 ml of water and treated with potassium carbonate. The supernatant oily base was repeatedly extracted with ether and dried with calcined magnesium sulfate. After the ether had been removed, the product was distilled in vacuo (b.p. 78-80° at 4 mm) and converted to the hydrochloride. After crystallization there was obtained 3.5 g of the hydrochloride of the phenylacetate.

*Students L. D. Bogatyreva and G. N. Dudnik participated in the experimental work.

Cinnamic ester of 1,2,5-trimethyl-4-ethynyl-4-piperidol (γ-isomer) (XIII). To 10 g of the γ-isomer of 1,2,5-trimethyl-4-ethynyl-4-piperidol was added 13 g of fused cinnamyl chloride. The reaction mass was heated for 1.5 hr at 120-125°. The reaction product was crushed to a powder under anhydrous ether, washed with ether until the odor of the acid chloride had disappeared, filtered, and dried in a vacuum desiccator. Recrystallization gave 8.15 g of the hydrochloride of the cinnamic ester.

β-Phenylpropionate of 1,2,5-trimethyl-4-ethyl-4-piperidol (γ-isomer) (XVIII). A solution of 2.6 g of hydrochloride of the cinnamic ester (XIII) (m.p. 205-207°) in 100 ml of methanol was placed in a hydrogenation flask and shaken in a hydrogen atmosphere with 0.5 g of Raney nickel. The volume of hydrogen absorbed was 560 ml (21°, 738 mm) compared with a theoretical requirement of 573 ml; the catalyst was filtered out and the methanol taken off in vacuo. The oily residue was crushed to a powder under anhydrous ether, filtered, and recrystallized from acetone to give 1.84 g of the hydrochloride of the γ-phenylpropionate.

Phenoxyacetate of 1,2,5-trimethyl-4-acetyl-4-piperidol (γ-isomer) (XXIV). A mixture of 5 g of the γ-isomer of 1,2,5-trimethyl-4-acetyl-4-piperidol (m.p. 59-60°) [5] and 10 g of phenoxyacetyl chloride in 15 ml of dry benzene was heated for 6 hr on a boiling water bath. The product was crushed to a powder under absolute ether, washed with ether until the odor of the acid chloride had disappeared, filtered, and twice recrystallized from absolute alcohol. There was obtained 5.6 g of the hydrochloride of the phenoxyacetate.

Acetate of 1,2,5-trimethyl-4-acetyl-4-piperidol (β-isomer) (XXI). A mixture of 20 g of the β-isomer of the ketol (m.p. 129-130°) [5] and 150 ml of acetic anhydride was heated for 4 hr on a boiling water bath. The excess acetic anhydride was removed in vacuo, and the residue was dissolved in 50 ml of water and treated with potassium carbonate. The oily product was repeatedly extracted with ether and dried with calcined magnesium sulfate. After the ether had been driven off, the residue was distilled in vacuo to give 21.5 g of the acetate.

SUMMARY

Syntheses were carried out of 25 esters of stereoisomeric 1,2,5-trimethyl-4-ethynyl-, 1,2,5-trimethyl-4-ethyl-, and 1,2,5-trimethyl-4-acetyl-4-piperidols which were needed for tests of their anesthetizing activity in radical and infiltrational anesthesia. The compounds are analogs of the anesthetics α- and β-eucaines.

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FORMATION OF CYCLOPENTANOLONES BY CYCLIZATION OF DIVINYL KETONES

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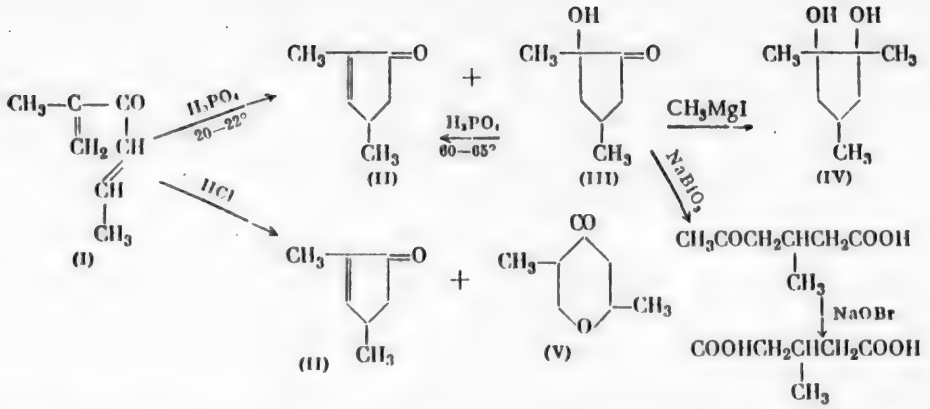
An extensive study has been made over a number of years in our laboratory of the cyclization of divinyl ketones which are obtained on hydration of divinylacetylenic hydrocarbons. It was shown that heating of these dienones with phosphoric acid led to high yields of cyclopentenones [1]. Cyclization of divinyl ketones lacking a free hydrogen in one of the vinyl radicals also leads to cyclopentanones but with the olefinic bond in another position [2].

In a study of cyclization of several divinyl ketones we showed that when milder temperature conditions are employed (15-20°) the corresponding cyclopentenones are again formed but they are accompanied by cyclic ketoalcohols (cyclopentanolones). The latter are readily dehydrated to cyclopentenones when heated with phosphoric acid. On this basis it was earlier suggested that the hydroxyl group in these ketoalcohols is in the β-position to the keto group [3].

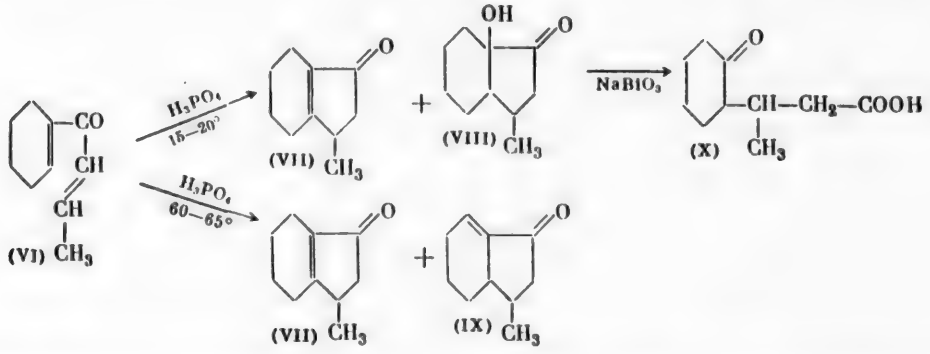
In our present work we aimed at making a more detailed study of this reaction with other starting substances, and also at a stricter proof of the position of the hydroxyl group in the ketoalcohols obtained. This would also afford an insight into the mechanism of their formation. The starting substance selected was propenylisopropenyl ketone (I), which is readily accessible. Treatment of the latter with phosphoric acid at 20-22° gave, in addition to 2,4-dimethylcyclopenten-2-one-1 (II), the crystalline 2,4-dimethylcyclopentanol-2-one-1 (III) in a yield of 15-20%. Identification of the structure of the latter is described below. Ketoalcohol (III) is soluble in water, does not decolorize a solution of bromine in chloroform, has a labile hydrogen, and readily forms a dinitrobenzoate. The presence of a keto group is confirmed by formation of a semicarbazone and a 2,4-dinitrophenylhydrazone, as well as by the infrared spectrum (1749 cm^{-1} band, which is characteristic of a keto group in a five-membered ring).

The structure of ketoalcohol (III) was confirmed by dehydration and oxidation. It splits off water with facility when heated with phosphoric acid and gives cyclopentenone (II). Treatment of (III) with phosphoric acid at room temperature does not lead to dehydration. Oxidation with sodium bismuthate by the procedure of [4] gives the known 3-methyl-4-acetylbutyric acid, which on oxidation with alkali hypobromite forms β-methylglutaric acid. It has thus been demonstrated that the hydroxyl group of ketoalcohol (III) is in the α-position of the CO group. Ketoalcohol (III) reacts with Grignard reagent but the reaction product (IV) could not be isolated pure.

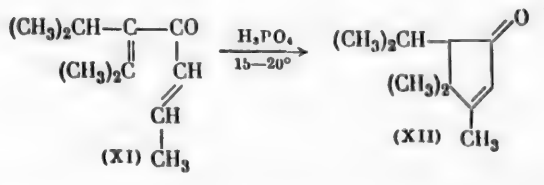
Numerous attempts to improve the yield of ketoalcohol (III) were unsuccessful. Performance of the reaction with more dilute acids (especially hydrochloric) gave, apart from cyclopentenone (II), a considerable quantity of 2,5-dimethyltetrahydro-4-pyrone (V). Formation of tetrahydro-γ-pyrones during cyclization of divinyl ketones has also been observed previously [5].



Treatment of propenyl-Δ^1-cyclohexenyl ketone (VI) with phosphoric acid at room temperature gives 1-methyl-4,5,6,7-tetrahydroindanone-3 (VII) together with a 10% yield of crystalline 1-methylhexahydroindanol-9-one-3 (VIII). Ketoalcohol (VIII) does not decolorize a solution of bromine in chloroform, does not undergo hydrogenation, and readily forms a dinitrobenzoate, semicarbazone, and 2,4-dinitrophenylhydrazone. It is easily dehydrated on heating with phosphoric acid and gives the previously described hydrindanone (VII) in high yield. Dehydration with potassium bisulfate leads to a mixture of isomeric hydrindanones (VII) and(IX), which are separated via the 2,4-dinitrophenylhydrazones. The ultraviolet spectra of the latter were identical and indicated the presence of one conjugated double bond. We also isolated hydrindanone (IX) from a mixture of the products of cyclization of dienone (VI) by heating with phosphoric acid. Linstead [6] also observed formation of isomers of this type during cyclohydration of 1,2-di-Δ^1-cyclohexenylacetylene [6]; we also observed it during cyclization of 1,2-di-Δ^1-cyclohexenylethanone [7]. Oxidation of ketoalcohol (VIII) with sodium bismuthate gave ketoacid (X).

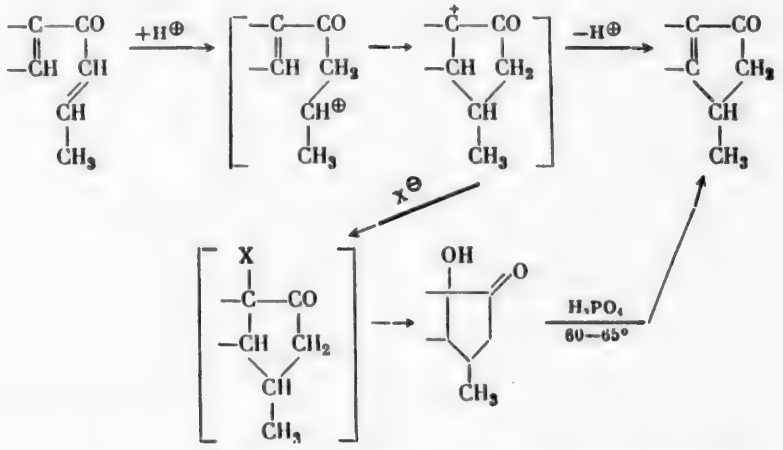


No success attended an attempt to effect cyclohydration of dienone (XI), which is deficient in a free hydrogen at one of the vinyl radicals (2-methyl-3-isopropylheptadien-2,5-one-4), to the corresponding ketoalcohol. Depending on the duration of the experiment and the acid concentration, the original dienone was recovered, or complete cyclization to 3,3,4-trimethyl-2-isopropylcyclopenten-4-one-5 (XII) occurred, or a mixture of the two substances was obtained.



In the preceding investigation we showed that treatment of 1,2-di-Δ^1-cyclohexeneylethanone with phosphoric acid at room temperature leads to 2-spirocyclohexylhexahydrochromanone-4; the corresponding ketoalcohol cannot be detected [7]. Consequently the direction of cyclization and cyclohydration of divinyl ketones depends not only on the reaction conditions but also on the structure of the original dienone.

It might be throught that cyclopentanolones are intermediates in formation of cyclopentenones since they are only obtained when the reaction is run under mild conditions. However, special experiments showed that these ketones are not dehydrated by phosphoric acid at 15-20°. Experiments also established that they are not formed by hydration of cyclopentenones, i.e., they are not secondary products. In all probability, the cyclization of divinyl ketones to cyclopentenones and their cyclohydration to cyclopentanolones proceed simultaneously, as follows:



The ionic intramolecular mechanism of cyclization of divinyl ketones to cyclopentenones represented in this scheme was previously confirmed by the deuteroexchange method [1, 8]. The cyclic carbonium ion, which loses a proton and forms the stable cyclopentenone, can probably also add on an anion X and undergo further transformation to cyclopentanolone.

EXPERIMENTAL

Propenylisopropenyl ketone (I) was prepared by the procedure described earlier and had the following constants: b.p. 51-52° (14 mm), $n^{20}D$ 1.4730 [9].

Cyclization of propenylisopropenyl ketone. Gradual addition of 26 g of phosphoric acid (d 1.27) was made to 26 g of stirred and cooled (ice water) dienone. The mass was left for 10 hr at 20-22°. It was then diluted with 20 ml of water, neutralized with sodium carbonate, and extracted with ether. The ethereal solution was dried with sodium sulfate. After three fractionations (at 10 mm) of the product from four similar experiments, the following fractions were collected: 1st, 40-50°, $n^{20}D$ 1.4680, 20 g; 2nd, 51-69°, $n^{20}D$ 1.4640, 22 g; 3rd, 70-77°, $n^{20}D$ 1.4565, 10 g; 4th, 78-80°, $n^{20}D$ 1.4560, 22 g.

The first fraction was mainly the original dienone (I); the second was mainly cyclopentenone (II). Redistillation of the 3rd and 4th fractions gave 30 g of colorless mobile liquid with a pleasant odor (b.p. 73-75° at 8 mm, 78-80° at 10 mm, $n^{20}D$ 1.4560, d^{20}_4 1.01), consisting of a mixture of 2,4-dimethylcyclopentanol-2-one-1 (III) and cyclopentenone (II). Freezing of this mixture yielded 12 g of pure crystalline ketoalcohol (III) with m.p. 34-35°, readily soluble in water; band at 1749 cm^{-1} in the infrared.

Found %: C 65.57, 65.52; H 9.23, 9.22. Number of active H atoms: 1.02, 1.02. $C_7H_{12}O_2$. Calculated %: C 65.59; H 9.37. Number of active H atoms: 1.

3,5-Dinitrobenzoate: m. p. 119-120° (from methanol).

Found %: C 52.29, 52.40; H 4.52, 4.51. $C_{14}H_{14}O_6N_2$. Calculated %: C 52.17; H 4.34.

2,4-Dinitrophenylhydrazone: yellow crystals, m.p. 106-107° (from aqueous alcohol); λ_{max} (in isooctane) 341 mμ.

Found %: N 17.99, 18.27. $C_{13}H_{16}O_5N_4$. Calculated %: N 18.18.

Semicarbazone: m.p. 181-182° (from water).

Found %: C 51.66, 51.72; H 8.13, 8.21. $C_8H_{15}O_2N_3$. Calculated %: C 51.88; H 8.10.

After being kept for several months, ketoalcohol (III) gave a mixture of 2,4-dinitrophenylhydrazones; numerous recrystallizations of the latter led to isolation of a pure product in the form of yellow crystals with m.p. 140-141°; λ_{max} (in isooctane) 341 mμ.

Found %: C 50.79, 50.76; H 5.29, 5.44. $C_{13}H_{16}O_5N_4$. Calculated %: C 50.65. H 5.19.

The mother liquor remaining after freezing-out of ketoalcohol (III) and storage in the refrigerator for two weeks was fractionally distilled to give 14 g of substance with b.p. 71-74° (8 mm), $n^{20}D$ 1.4560, and 1.5 g of a vitreous, transparent residue.* Hydrogenation of this substance in ethanol in presence of platinum oxide led to absorption of 200 ml of hydrogen, corresponding to a content of about 30% of cyclopentenone (II) in this mixture; 2,4-dimethylcyclopentanone 1-2,4-dinitrophenylhydrazone melted at 170-171° (from a mixture of alcohol and ethyl acetate).

Found %: C 53.44, 53.36; H 5.52, 5.49. $C_{13}H_{16}O_4N_4$. Calculated %: C 53.42; H 5.48.

Dehydration of 2,4-dimethylcyclopentanol-2-one (III). a) A mixture of 2.5 g of ketoalcohol (m.p. 33-34°) and 2.5 g of phosphoric acid (d 1.76) was heated for 1 hr at 65-70°. The reaction mixture was diluted with 5 ml of water, neutralized with sodium carbonate, and extracted with ether. The ethereal solution was dried with sodium sulfate. Fractional distillation yielded 1.2 g (60%) of cyclopentenone (II) with b.p. 65-67° (22 mm), $n^{20}D$ 1.4650; the 2,4-dinitrophenylhydrazone melted at 205-206° and did not give a depression in admixture with an authentic specimen.

b) The ketoalcohol (2.5 g) was left in contact with phosphoric acid (d 1.76) for 17 hr at 19-21°. The mass was worked up to give 1.5 g of the starting substance.

Oxidation of 2,4-dimethylcyclopentanol-2-one-1 (III). A mixture of 1 g of ketoalcohol (m.p. 34-35°), 8 ml of glacial acetic acid, 4 ml of $3\frac{1}{3}$ M phosphoric acid, and 1.5 g of sodium bismuthate was heated for 2 hr at 40-50° (the orange color of the pentavalent bismuth disappeared within 10-15 min after start of heating). The solution was filtered and neutralized with sodium carbonate; the neutral products were extracted with ether. Removal of the ether left 0.3 g of dark-yellow liquid with an acid reaction. The acid salts were decomposed with 5 ml of 5% hydrochloric acid and extracted with ether. The ethereal solution was dried with sodium sulfate. The residue (0.5 g) after removal of the ether was converted to a semicarbazone and 2,4-dinitrophenylhydrazone. The semicarbazone melted at 170-171° (from alcohol) and corresponded to the semicarbazone of 3-methyl-4-acetylbutyric acid.

Found %: C 47.69, 47.84; H 7.53, 7.53. $C_8H_{15}O_3N_3$. Calculated %: C 47.70; H 7.49.

Literature data [10]: m. p. 170-171°.

2,4-Dinitrophenylhydrazone: yellow crystals, m.p. 145-146° (from alcohol; λ_{max} (in isooctane) 344 mμ.

Ketoalcohol (III) is not oxidized by other oxidizing agents (chromic acid in acetone or acetic acid, or the pyridine complex).

Oxidation of 3-methyl-4-acetylbutyric acid. Bromine (6.6 g) was added to 1.8 g of the acid, 10 ml of water, and 3.2 g of sodium hydroxide with continuous stirring and with ice-water cooling. Bromoform and water were then distilled off. The acid salts were decomposed with 15 ml of concentrated hydrochloric acid. The mass was extracted with ether, the ether was driven off from the extract, and the residue (crystalline) was recrystallized from a mixture of chloroform and carbon disulfide. Yield 0.65 g of β-methylglutaric acid with m.p. 84-85°.

Reaction of 2,4-dimethylcyclopentanol-2-one-1 (III) with Grignard reagent. To the Grignard reagent prepared from 1.5 g of magnesium and 8 g of methyl iodide was added (with stirring) 3 g of ketoalcohol (III) in 25 ml of absolute ether. Heat was developed, and evolution of methane ceased after 20-25 min. The reaction mixture was heated for another 30 min at the boiling point of ether; it was decomposed with water and then with dilute (5-6%) hydrochloric acid and extracted with ether. The ethereal solution was washed with sodium bicarbonate and thiosulfate. Fractional distillation gave 1.7 g of diol (IV); a colorless, fairly viscous liquid with b.p. 84-86° (6 mm), $n^{20}D$ 1.4665; it was evidently impure 1,2,4-trimethylcyclopentanediol-1,2 (IV).

*The amount of vitreous fraction increased considerably if this substance was stored for two months.

Found %: C 66.13, 66.15; H 10.08, 10.25. $C_8H_{16}O_2$. Calculated %: C 66.60; H 11.10.

Cyclization of propenylisopropenyl ketone (I) under other conditions. a) A mixture of 21 g of dienone (I) and 42 g of hydrochloric acid (d 1.085) was stirred for 6 hours at 40-45°. The reaction products were diluted with 15 ml of water, neutralized with sodium carbonate and extracted with ether. The extract was dried with sodium sulfate. Fractional distillation gave 18 g of substance with b.p. 58-65° (10 mm), $n^{20}D$ 1.4575, consisting of a mixture of cyclopentenone (II) and 2,5-dimethyltetrahydropyrone-4 (V); these were identified through their 2,4-dinitrophenylhydrazones; m.p. 205-206° (no depression in admixture with an authentic derivative of the cyclopentenone) and m.p. 186-187°, golden needles, λ_{max} (in isooctane) 345 mμ.

Found %: C 51.02, 51.19; H 5.22, 5.15. $C_{13}H_{16}O_5N_4$. Calculated %: C 51.65; H 5.19.

No active hydrogen was detected in this mixture.

b) A mixture of 10 g of dienone and 13 ml of hydrochloric acid (d 1.085) was stirred for 2 hours at 70-75°. The product was worked up as above to give 7 g of substance with b.p. 48-50° (8 mm), $n^{20}D$ 1.4650, consisting mainly of cyclopentenone (II); the 2,4-dinitrophenylhydrazone melted at 204-205° and the melting point was not depressed in admixture with an authentic specimen.

c) A mixture of 7 g of dienone and 15 ml of hydrochloric acid (d 1.18) was stirred for 6 hours at 20-25°. After working up, the product was fractionated to give 8 g of a mixture of chlorine-containing product; b.p. 55-85° at 8 mm, $n^{20}D$ 1.4680. Reaction with 2,4-dinitrophenylhydrazone established that the mixture contained mainly 2,5-dimethyltetrahydro-4-pyrone (V) (hydrazone with m.p. 186-187°) and cyclopentenone (II) (hydrazone with m.p. 204-205°). In both cases no depression in admixture with the specimens described above.

d) A mixture of 7.5 g of dienone and 15 ml of hydrochloric acid was stirred for 6 hours at 40-45°. The product was worked up and fractionally distilled to give the following fractions: 1st, 70-78° (29 mm), $n^{20}D$ 1.4720, 5.4 g; 2nd, 67-70° (7 mm), $n^{20}D$ 1.4730, 0.8 g. The main product in both fractions, identified through the 2,4-dinitrophenylhydrazone, was cyclopentenone (II).

e) A mixture of 10 g of dienone (II) and 10 g of phosphoric acid (d 1.8) was kept at 15-16° for 23 hours. Further treatment as above followed by fractionation gave 7 g of cyclic ketone with b.p. 49-50° (8 mm), $n^{20}D$ 1.4675.

Action of phosphoric acid on cyclopentenone (II). 5 g of cyclopentenone (b.p. 49-50° at 8 mm, $n^{20}D$ 1.4675) was left in contact with phosphoric acid (d 1.76) for 5 hours; the product was worked up and fractionated to give 4 g of the original cyclopentenone.

Cyclization of propenyl-Δ^1-cyclohexenyl ketone (VI) at room temperature. Propenyl-Δ^1-cyclohexenyl ketone was prepared by the earlier method [11] and had the following constants: b.p. 111-112° (12 mm), $n^{20}D$ 1.5150. Into 40 g of dienone (cooled with ice water) was stirred 40 g of phosphoric acid (d 1.76). Stirring at 15-20°• was then continued for 4.5 hours. The reaction mixture was worked up as described above and fractionated to give 15 g of substance with b.p. 105-109° (5 mm), $n^{20}D$ 1.5045, and 10 g of substance with b.p. 110-111° (4 mm), $n^{20}D$ 1.5021. Freezing of both fractions in solid carbon dioxide led to separation of 4 g of snow-white acicular crystals with m.p. 71-72° (from isooctane), consisting of pure 1-methylhexahydroindanol-9-one-3 (VIII).

Ultraviolet spectrum: λ_{max} (in ethanol) 300 mμ; ϵ_{max} 1.482.

Infrared spectrum: 1746 cm^{-1}.

Found %: C 71.42, 71.63; H 9.70, 9.75. No. of active H: 1.1, 0.96. $C_{10}H_{16}O_2$. Calculated %: C 71.39; H 9.58. No. of active H: 1.

3,5-Dinitrobenzoate: m.p. 146-147° (from methanol).

Found %: C 56.09, 56.04; H 4.92, 4.87. $C_{17}H_{18}O_2N_2$. Calculated %: C 56.35; H 4.90.

2,4-Dinitrophenylhydrazone: m.p. 168-169° (from aqueous alcohol).

Ultraviolet spectrum: λ_{max} (isooctane) 341 mμ; ϵ_{max} 1.8000; λ_{max} (in ethanol) 360 mμ.

Found %: C 55.35, 55.11; H 5.86, 5.80; N 16.09, 16.09. $C_{16}H_{20}O_5N_4$. Calculated %: C 55.16, H 5.59; N 16.08.

•At 5-10° nearly the whole of the dienone was recovered unchanged.

The semicarbazone melted at 195-197° (from alcohol). The mother liquor (16.8 g) was fractionally distilled after separation of the crystals. There was obtained 14 g of substance with b.p. 100-108° (5 mm) $n^{20}D$ 1.5070. Heating of this product with phosphoric acid (d 1.7) for 2 hr at 60° resulted in separation of 13 g of substance with b.p. 96-98° (3 mm), $n^{21}D$ 1.5090, consisting mainly of the hydridanone (VII) together with a minute amount of top fraction boiling up to 96° and with $n^{20}D$ 1.5000. The 2,4-dinitrophenylhydrazone of this fraction had m.p. 224-225° (from a mixture of ethanol and benzene) and was evidently a mixture of the 2,4-dinitrophenylhydrazones of the hydrindanones (VII and IX).

Dehydration of 1-Methylhexahydroindanol-9-one-3 (VIII).

a) With phosphoric acid. A mixture of 1.8 g of ketoalcohol (m.p. 71-72°), 5 ml of phosphoric acid (d 1.76), and 10 ml of isooctane was stirred for 2 hr at 60-65°. The isooctane was distilled off and stirring continued at the same temperature for another hour. The reaction mixture was diluted with 5 ml of water, neutralized with sodium carbonate and extracted with ether. Fractional distillation gave 1.2 g of cyclic ketone (VII) with b.p. 78-79° (1 mm), $n^{18}D$ 1.5130; the 2,4-dinitrophenylhydrazone melted at 243° and did not give a depression in admixture with an authentic specimen [11].

b) With potassium bisulfate. A mixture of 0.5 g of ketoalcohol and 0.2 g of calcined potassium bisulfate was heated for 45 min at 155-160°. From the reaction product (after cooling) was obtained 0.9 g of a mixture of 2,4-dinitrophenylhydrazones with m.p. 228-230°. Numerous fractional recrystallizations of this mixture yielded the 2,4-dinitrophenylhydrazones: of hydrindanone (VII) with m.p. 243° and of hydrindanone (IX) with m.p. 218-219° (in smaller amount); the latter did not give a depression in admixture with the specimen described below.

Oxidation of hydrindanone (VIII) with sodium bismuthate. A mixture of 0.5 g of ketoalcohol, 4 ml of glacial acetic acid, 2 ml of 3 1/3 M phosphoric acid, and 0.75 g of sodium bismuthate was stirred for 2 hr at 40-45°. The solution was filtered, the acetic acid distilled off, and the residue neutralized with sodium carbonate and extracted with ether. No neutral products were found after the ether had been taken off. The acid salts were decomposed with 5 ml of 10% hydrochloric acid and the acid extracted with ether. From the noncrystallizing residue (0.6 g) was obtained a semicarbazone with m.p. 186-187° (decomp.) (from alcohol).

Found %: C 54.49, 54.28; H 7.93, 7.85. $C_{11}H_{19}O_3N_3$. Calculated %: C 54.76; H 7.88.

The 2,4-dinitrophenylhydrazone melted at 170-171° (from alcohol), λ_{max} (in heptane) 348.5 mμ.

Cyclization of propenyl-Δ^1-cyclohexenyl ketone (VI) by heating. A mixture of 33 g of dienone (VI) (b.p. 107-109° at 7 mm, $n^{20}D$ 1.5113) and 38 g of phosphoric acid (d 1.79) was stirred for 6 hr at 60-65°. The product was worked up and fractionally distilled to give 30 g of substance with b.p. 117-118° (30 mm), $n^{17}D$ 1.5134. Fractional distillation of this substance in a 24-plate column gave the following fractions: 1st 132-137°, $n^{20}D$ 1.5052, d^{20}_4 1.0062, 5.5 g; 2nd 137-140°, $n^{20}D$ 1.5080, d^{20}_4 1.0080, 5.2 g; 3rd 140.5-141°, $n^{20}D$ 1.5144, d^{20}_4 1.0135, 13.5 g.

From the 1st fraction was isolated mainly the 2,4-dinitrophenylhydrazone of hydrindanone (IX) with m.p. m.p. 218-219° (from a mixture of ethanol and ethyl acetate); λ_{max} (in isooctane) 355, 372, 386 mμ.

Found %: C 58.1; H 5.53; N 16.98. $C_{15}H_{18}O_4N_4$. Calculated %: C 58.17; H 5.45; N 16.97.

The 3rd fraction was pure hydrindanone (VII) [11]; the 2,4-dinitrophenylhydrazone melted at 246-247° and did not give a depression in admixture with an authentic specimen; λ_{max} (in isooctane) 359, 376, 393 mμ.

Hydrolysis of the semicarbazone of hydrindanone (VII). A mixture of 1.5 g of semicarbazone (m.p. 213-214°), 10 ml of benzene, and 10 ml of 10% sulfuric acid was heated for 1 hr at 70-80°. There was obtained 0.8 g (80%) of hydrindanone (VII) with b.p. 127-128° (19 mm), $n^{20}D$ 1.5144.

2-Methyl-3-isopropyl-2,5-heptadien-4-one (XI) was obtained by the procedure described earlier and had the following constants: b.p. 84-84.5° (8 mm), $n^{20}D$ 1.4735 [12].

Attempts to cyclohydrate dienone (XI). a) A mixture of 10 g dienone (b.p. 84-84.5° at 8 mm, $n^{20}D$ 1.4735) and 10 g of phosphoric acid (d 1.7) was stood at 19-20° for 1.5 hr. The product was worked up and fractionated to give 9 g of the original dienone.

b) A mixture of 5 g of dienone and 5 g of phosphoric acid (d 1.76) was left for 6 hr at 20°. The product was worked up and fractionated to give 5 g of the previously described 3,3,4-trimethyl-2-isopropylcyclopenten-4-one-1 (XII) with b.p. 100° (8 mm), $n^{20}D$ 1.4780 [2].

c) A mixture of 8 g of dienone and 8 g of phosphoric acid (d 1.76) was left for 2 hr at 18-20°. The product was worked up and fractionally distilled to give a mixture of the original dienone (XI) and the cyclopentenone (XII).

SUMMARY

1. It was shown that treatment of propenylisopropenyl ketone and propenyl-Δ^1-cyclohexenyl ketone with phosphoric acid at 15-20° led not only to their cyclization to 2,4-dimethylcyclopenten-2-one-1 and 1-methyl-4,5,6,7-tetrahydroindanone-3 but also to the cyclohydration of these dienones to 2,4-dimethylcyclopentanol-2-one-1 and 1-methylhexahydroindanol-9-one-3, respectively. On heating with phosphoric acid, the last-named compounds easily dehydrate with formation of cyclopentenone and hydrindanone, respectively.

2. A possible mechanism of cyclohydration of divinyl ketones to α-cyclopentanolones is put forward.

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THE SIMPLEST ANALOGS OF CORTICOSTEROIDS

IX.• STEREOCHEMISTRY OF NUCLEOPHILIC ADDITION TO THE CARBONYL GROUP. 6. THE STERIC DIRECTIVITY OF THE CYANOHYDRIN AND ORGANOMETALLIC SYNTHESES ON THE BASIS OF 3-METHYLCYCLOHEXANONE

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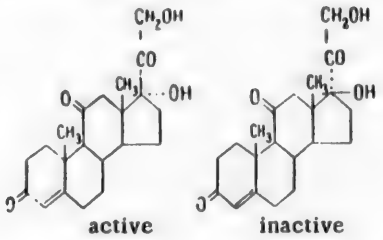
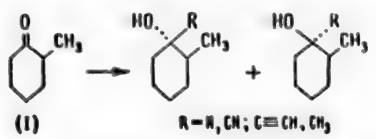
The biological activity of steroids is known to depend in great measure on the steric configuration of the substituents in the ring [1, 2]. Biologically active corticosteroids, for example, have the 17-side chain in the β-position. Activity is also exhibited by androgenic and estrogenic hormones with a β-configuration of the 17-hydroxyl group. Change of configuration leads to a sharp drop or complete disappearance of their activity. Similar effects arise when substituents are in other positions in a steroid molecule.



active inactive

In the course of our study over a number of years of the synthesis of the simplest analogs of corticosteroids [3], during which we developed methods of introducing a corticoidic side chain, we were compelled to study the stereochemistry of introduction of oxidic side chains into cyclic compounds. For this purpose we started from compounds of the cyclohexane series. Our immediate objective was the clarification of the stereochemistry of nucleophilic addition to the carbonyl group of cyclic ketones, with special reference to steric directivity of the cyanohydrin, acetylenic, and organometallic syntheses in a series of substituted cyclohexanones. In the case of 2-methylcyclohexanone (I) we had shown [4] that all of the above reactions are associated with a definite but varying steric selectivity. Reaction of ketone (I) with acetone cyanohydrin [4, 5], for example, leads to a mixture of cyanohydrins containing 75-80% of cis-form and 25-20% of trans-form, whereas the acetylenic synthesis with (I) under pressure leads to a mixture containing 60% of cis-form and 40% of trans-form. On the other hand, reaction of methylmagnesium iodide with (I) leads to a mixture containing 25% of cis-form and 75% of trans-form.



(I) R = H, CN; C≡CH, CH3

•Communication VIII in this series: [11] Izvest. Akad. Nauk SSSR 750 (1959).

These results are fully consistent with information in the literature about ionic nucleophilic reduction of ketone (I) (Table 1).

TABLE 1

Steric Directivity of Nucleophilic Addition to the Carbonyl Group of 2-Methylcyclohexanone

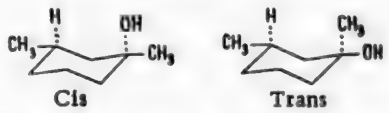
Reagent	Substituent introduced	Content in mixture (in %)* of cis-form	Content in mixture (in %)* of trans-form	Literature references
Na in alcohol or moist ether	H	99—72	1—28	[6]
$(CH_3)_2C(OH)CN$ or KCN	CN	80—75	25—20	[4,7]
HCN (anhydrous) . . .	CN	69	31	[7]
$LiAlH_4$	H	82—60	18—40	[5,8]
$CH{\equiv}CH$	$C{\equiv}CH$	60	40	[4]
CH_3MgI	CH_3	25	75	[4]

*The configuration is governed by the entering substituent.

It was shown by spectrographic [9] and chemical methods [10] that in the cis-compounds that we obtained, substituents introduced and present have predominantly 1a2e conformation, whereas in the trans-compounds the 1e2e conformation predominates.

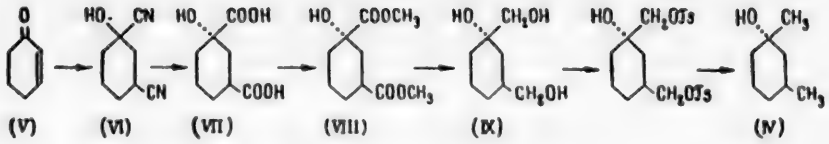
It was of interest to establish whether these steric characteristics also apply to 3-methylcyclohexanone (II). With this objective we embarked on a study of the stereochemistry of the cyanohydrin and organometallic syntheses starting from 3-methylcyclohexanone (II) [11].

The literature [12] mentions only cis- and trans-1,3-dimethylcyclohexanols (III) and (IV) as examples of compounds of the 1,3-disubstituted cyclohexanol series that can be synthesized without change of configuration, so that unequivocal proof is obtained of their steric structure. The configuration of the latter was proposed on the basis of the observation that alcohol (IV) has a higher rate of dehydration under the action of formic acid, and also on the basis of the Auwers-Skita rule [higher values of refractive index, density and boiling point for alcohol (III)]. However the configuration assigned to alcohols (III) and (IV) is evidently wrong and should be reversed, just as was necessary in the case of the 1-methylcyclohexanols-3 [13]. Actually, conformational analysis predicts that the predominant conformation for the cis-alcohol must be the 1e, 3e-dimethyl-1a-hydroxy conformation, and for the trans-alcohol, the 1a,3e-dimethyl-1e-hydroxy conformation. Consequently the former must have the higher rate of dehydration (diaxial trans-elimination) [14]. At the same time the higher values of refractive index, density and boiling point must be attributed to the second compound since it contains a bulkier axial substituent (CH_3) and an equatorial hydroxyl group [15].



Cis Trans

We confirmed these assumptions by the following transformations. Condensation of cyclohexanone (V) with acetone cyanohydrin gave 1,3-dicyanocyclohexanol (VI), possibly in the form of a mixture of the two isomers. The reaction product could not be purified since it decomposed during distillation in vacuo. Hydrolysis of the dinitrile (VI) with a mixture of hydrochloric and acetic acids saturated with hydrogen chloride gave an oily mixture of products from which the crystalline cyclohexanol-1,3-dicarboxylic acid (VII) was separated; m.p. 133.5-134°. This acid did not give a lactone on heating with a mixture of acetic and hydrochloric acids. The cis-configuration (1e,3e-conformation of the carboxyl groups) can be assigned to it since we know that only cis-cyclohexanol-1-carboxylic-3-acids are susceptible to lactonization under these conditions [16].



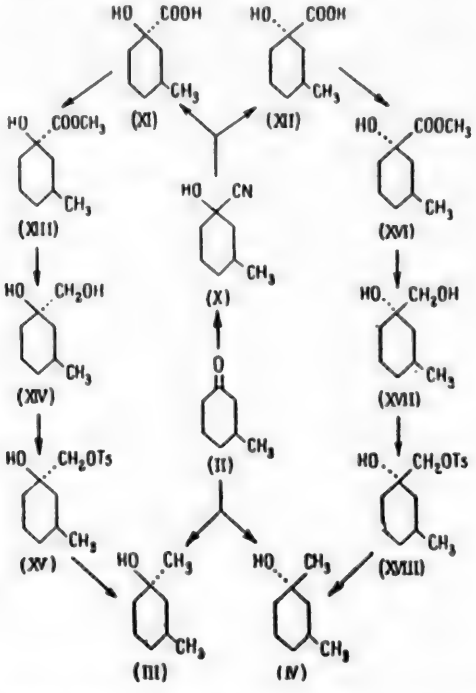
The dimethyl ester of the cis-acid (VIII), prepared with the help of diazomethane, was reduced in the unpurified form with lithium aluminum hydride to give the triol (IX), which was then treated in the cold with p-toluenesulfochloride in pyridine and subsequently reduced with lithium aluminum hydride [17]. This gave cis-1,3-dimethylcyclohexanol which was identical with alcohol (IV), to which was previously assigned (erroneously) the trans-configuration [12]. It was thus established that alcohol (III) indeed has trans-configuration and alcohol (IV) cis-configuration.* This result is also confirmed by spectral data [18].

Reaction of ketone (II) with acetone cyanohydrin yields a liquid mixture of cis- and trans-1-cyano-3-methylcyclohexanols (X). Saponification of the latter with a mixture of acetic and hydrochloric acids saturated with hydrogen chloride gave a mixture of trans- and cis-3-methylcyclohexanol-1-carboxylic acids (XI) and (XII) in 95% yield. The latter were separated via the barium salts, which differed in solubility, and by subsequent recrystallization of acid mixtures enriched with one isomer or the other. These operations were repeated several times. The ratio of isomers in the residue was evaluated from the composition of the separated portion. In this manner it was established that the mixture of acids contains approximately 75% of trans-acid (XI) with m.p. 54.5-55° and 25% of cis-acid (XII) with m.p. 104.5-105°. This result was checked by refractometric measurements. For this purpose the starting mixture of acids was esterified with diazomethane and the refractive index of the mixture of dimethyl esters determined. The composition of the mixture was calculated from the formula

$$100 \times n^{20}D\,(mi) = C \times n^{20}D\,(c) + T \times n^{20}D\,(t);\ C + T = 100,$$

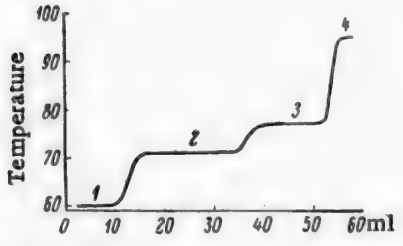
in which C and T are the % contents of cis- and trans-forms, and mi, c and t relate respectively to the refractive indices of the mixture, the cis-form and the trans-form. On this basis the mixture contains 76% of trans- and 24% of cis-form, in good agreement with the result by the former method.

Acid (XII) with m.p. 103-104° was previously obtained by hydrolysis of 1-bromo-3-methylcyclohexanecarboxylic acid [19]. Subsequently, hydrolysis of the mixture of cyanohydrins (X) gave [20] two hydroacids with m.p. 99 and 75°; they are both evidently impure forms of acid (XII).



*During a visit to Moscow in 1958, Prof. Chiurdoglu expressed his agreement with out views about the configuration of alcohols (III) and (IV).

Proof of the configuration of acids (XI) and (XII) was obtained by their conversion to 1,3-dimethylcyclohexanols (III) and (IV) without the asymmetric center being affected. For this purpose the trans-acid (XI) was converted to the methyl ester (XIII) and the latter reduced by lithium aluminum hydride to the trans-1-hydroxymethyl-3-methylcyclohexanol-1 (XIV). Treatment of the liquid diol (XIV) with p-toluenesulfochloride in pyridine gave the liquid monotosylate (XV) which without purification was subjected to further reduction with lithium aluminum hydride [17] in a mixture of ether and benzene. The product was trans-1,3-dimethylcyclohexanol (III) with m.p. 25-26°. A similar series of transformations was realized with the cis-acid (XII); the methyl ester (XVI) was reduced with lithium aluminum hydride to cis-1-hydroxymethyl-3-methylcyclohexanol (XVII) with m.p. 72-73°. Tosylation of the latter and reduction of the tosylate (XVIII) gave cis-1,3-dimethylcyclohexanol (IV) which was found to be identical with alcohol (IV) obtained by other methods.



Distillation curve: 1) ketone (II), 2) cis-alcohol (IV), 3) trans-alcohol (III), 4) n-octyl alcohol.

Reaction of ketone (III) with methylmagnesium iodide under the usual conditions gave a mixture of alcohols (III) and (IV). After addition of ketone (II) and the high-boiling n-octyl alcohol, the mixture was fractionated in a 35-plate column and the pure forms of alcohols (III) and (IV) were collected. They were identical with the products described above. Judging by the distillation curve (see diagram) the original mixture consists of 40% of trans-alcohol (III) and 60% of cis-alcohol (IV).

Data for the steric directivity of nucleophilic addition to the carbonyl group of 3-methylcyclohexanone are set forth in Table 2.

Study of the Raman spectra shows [9, 18] that the predominant conformations in 1,3-disubstituted cyclohexanols are 1a3e-conformations

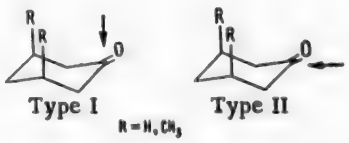
TABLE 2

Steric Directivity of Nucleophilic Addition to the Carbonyl Group of 3-Methylcyclohexanone

Reagent	Substituent introduced	Content in mixture (%)		Literature references
		trans-form	cis-form	
Na	H	80—78	20—22	[6, 21] *
$LiAlH_4$	H	94—89	6—11	[6, 8] *
$(CH_3)_2C(OH)CN$ . .	CN	75	25	
CH_3MgI	CH_3	40	60	

* Configuration corrected on the basis of literature data [13].

of the introduced and existing substituents in the trans-series and 1e3e-conformation of the introduced and existing substituents in the cis-series. The only exception appears to be cis-1,3-dimethylcyclohexanol in the absence of a solvent. Inspection of Tables 1 and 2 reveals that, ignoring certain qualitative differences, all the reactions can be classed in one of two stereochemical groups. The cyanohydrin and acetylenic syntheses, as well as alkaline reduction, lead to predominant ae-conformation, whereas the organometallic synthesis leads predominantly to ee-conformation. In the former case, therefore, axial entry of the substituent (H, CN, C ≡ CH) predominates, but in the second case entry of the substituent (CH_3) in the equatorial position predominates.



It is important to note that a similar picture arises with the majority of ketosteroids. For example, the action of methylmagnesium halides on 17a-keto-D-homosteroids leads to formation exclusively of 17aα-hydroxy-D-homosteroids (a-conformation of the hydroxyl group) [22], whereas the main products of reduction of such ketones with sodium borohydride [23] and the main products of the acetylenic synthesis [22, 24] are 17aβ -hydroxy-D-homosteroids (e-conformation of the hydroxyl group). In the cyclohexane series a similar directivity is found with 4-tert -butylcyclohexanone [25]. It may be suggested that axial entry of substituents is determined by the polar orientation factor of the nucleophilic reagent, which depends on the mechanism of the ionic nucleophilic addition reaction, while equatorial entry is governed by the steric hindrance caused by the axial meta-substituents (including the hydrogen atoms).

EXPERIMENTAL

Cyclohexenone (V) was prepared by the literature method [26] with slight modifications. A mixture of 588 g of cyclohexanone and 1800 ml of water was treated with chlorine until the weight had increased by 430 g. The mass was stirred for an hour and extracted with ether. The extract was dried with magnesium sulfate and distilled to give 400.7 g of α-chlorocyclohexanone (b.p. 69-76° at 8 mm, $n^{19}D$ 1.4850), which was mixed (without purification) with 200 ml of ethylene glycol, 800 ml of benzene, and 1.5 g of p-toluenesulfonic acid and boiled for 7 days in connection with a water separator. This treatment led to separation of 66 ml of water. The mixture was treated with sodium carbonate, filtered, and evaporated in vacuo to give 543 g of residue—α-chlorocyclohexenone ketal. The crude ketal (85 g) was stirred with 70 g of potassium hydroxide powder and 150 ml of ethylene glycol while heating to 192°. During this operation, a mixture of water, ketal, and glycol distilled over. The distillate was extracted with ether, dried with calcium chloride, and distilled. There was obtained 30.9 g of cyclohexenone ketal with b.p. 57-59° (6 mm), $n^{19}D$ 1.4782. A mixture of 208 g of the unsaturated ketal and 180 ml of 5% hydrochloric acid was heated and stirred until homogeneous and then slowly cooled. It was then neutralized with sodium bicarbonate, extracted with ether, dried with sodium sulfate, and distilled to give 100 g of cyclohexenone (V) with b.p. 48-51° (7.5 mm), $n^{20}D$ 1.4865 [26].

Preparation and hydrolysis of 1,3-dicyanocyclohexanol (VI). A mixture of 19.2 g of cyclohexenone (V), 85 g of acetone cyanohydrin, and 50 ml of saturated methanolic solution of potassium carbonate was stood overnight at 20°; it was then acidified with sulfuric acid until it had an acidic reaction and evaporated in vacuo. The excess of acetone cyanohydrin (48 g) was taken off in vacuo (4 mm) at 52-53°. The residue was dissolved in ether, washed with saturated sodium chloride solution and with water, dried, and treated with active carbon. Removal of the ether left 23.2 g of hydroxydinitrile (VI) in the form of an oil that did not distil without decomposition. The reaction product was dissolved in 60 ml of glacial acetic acid and 80 ml of concentrated hydrochloric acid, saturated for an hour with hydrogen chloride, and stood for three weeks at 20°. The mixture was then refluxed for 3 hr and evaporated to dryness. The residue was dissolved in 200 ml of saturated sodium carbonate solution, extracted with ether, and acidified with 15% hydrochloric acid until it had a strongly acidic reaction. The resulting oil was extracted with ether in a percolator for 5 days, and the ether extract dried with sodium sulfate and evaporated to give 23.1 g of crystallizing oil. Crystallization from benzene and nitromethane gave 14 g of cyclohexanol-1-dicarboxylic acid-1,3 (VII) with m.p. 133.5-134° [27].

Found %: C 50.83, 50.83; H 6.55, 6.47. $C_8H_{12}O_5$. Calculated %: C 51.06; H 6.38.

Titration with 0.1 N alkali showed the presence of two carboxyl groups.

Preparation and reduction of the methyl ester of hydroxydiacid (VIII). To a diethyl ether solution of eleven and three-tenths grams of hydroxydiacid (VII) was added a diethyl ether solution of diazomethane (from 35 g of nitrosomethylurea); the mixture was left for 2 hr at 20°, dried with sodium sulfate and evaporated. There was obtained 11.4 g of methyl ester (VIII) in the form of an undistillable oil; the solution of the latter in 70 ml of ether was stirred into a suspension of 6.1 g of lithium aluminum hydride in 300 ml of ether. After heat evolution had ceased, the mass was stirred at the boil for another 17 hr, treated with 40 ml of ethyl acetate, and with dilute sulfuric acid with cooling. The weakly acidic mixture was neutralized with solid sodium bicarbonate, filtered, dried with sodium sulfate, and evaporated. The residue consisted of 4 g of noncrystallizing oil. It was dissolved in 40 ml of anhydrous pyridine and cooled to 0°; addition was then made in portions of 11.5 g of p-toluenesulfochloride. The solution was left for 48 hr at -3 to -4° and then diluted with 120 ml of saturated sodium bicarbonate solution and extracted six times with ether. The ethereal extract was washed with dilute sulfuric acid, water and, bicarbonate solution. It was then dried and the ether taken off to leave 8.1 g

of oil. To a suspension of 4.5 g of lithium aluminum hydride in 150 ml of ether and 100 ml of benzene was added a solution of 8.1 g of unpurified tosylate in 75 ml of benzene. The temperature rose to 35° during the operation. After completion of the addition, the mixture was boiled for 24 hr, and treated with 23 ml of ethyl acetate and with dilute sulfuric acid; it was then neutralized with solid sodium bicarbonate, dried with sodium sulfate, and distilled to give 1.2 g of cis-1,3-dimethylcyclohexanol (IV), b.p. 72.5° (21 mm), $n^{20}D$ 1.4540, identical with the product obtained by another route [12].

3,5-Dinitrobenzoate: m.p. 118-119° (from ligroine); no depression in a mixed melting test with a specimen prepared by another route.

3-Methylcyclohexanone (II) was prepared by the literature procedure [28] slightly modified. To 1300 g of ethyl acetoacetate and 150 g of paraformaldehyde, with stirring and cooling, was added 25 ml of piperidine in the course of an hour while the temperature was held at 54-55°; following this the mixture was heated at 55-60° for another 30 min and stood overnight at 20°. Yield of crude product 1400 g.

A mixture of 500 g of this product, 250 ml of acetic acid, 80 ml of concentrated sulfuric acid, and 300 ml of water was stirred at the boil for 6 hr, partially neutralized, and extracted three times with ether. The product was finally neutralized with sodium carbonate, dried with sodium sulfate and distilled to give 111 g of 3-methylcyclohexenone with b.p. 64-66° (7 mm), $n^{20}D$ 1.4900.

Hydrogenation of 270.4 g of 3-methylcyclohexenone was effected in 250 ml of alcohol over 0.4 g of platinum oxide. In the course of 11 hr 10 min, 54.5 liters of hydrogen was taken up, after which the rate of hydrogenation fell abruptly. The mass was filtered, treated with sodium bicarbonate, and distilled in a 35-plate column to give 228.9 g of ketone (II) with b.p. 55.8-56.4° (16 mm), $n^{20}D$ 1.4454 [26].

Preparation of a mixture of 1-cyano-3-methylcyclohexanols (X). A mixture of 11.2 g of ketone (II), 17 g of acetone cyanohydrin, and 10 ml of saturated methanolic potassium carbonate was left overnight at 20°, acidified with concentrated sulfuric acid to a weakly acidic reaction, and fractionally distilled. There was recovered 8.7 g of the acetone cyanohydrin (b.p. 47-60° at 3.5 mm), and 12.2 g of a mixture of cyanohydrins (X) was obtained; b.p. 92-93.5° (3.5 mm), $n^{19}D$ 1.4602 [29].

Hydrolysis of mixture of cyanohydrins (X). A solution of 28 g of (X) in 120 ml of glacial acetic acid and 160 ml of hydrochloric acid was saturated with hydrogen chloride for an hour and then stood for 7 days at 20°. The solution was refluxed for 3 hr and evaporated to dryness. The residue was treated with 150 ml of saturated sodium carbonate solution, heated for 2 hr on a boiling water bath, cooled and acidified with hydrochloric acid until the liquid had an acidic reaction. The resulting oil was extracted with ether in a percolator for three days. The extract was dried with magnesium sulfate and evaporated to give 30.2 g of the mixture of acids (XI) and (XII) in the form of an oil.

Separation of mixture of acids (XI) and (XII). A solution of 25.4 g of the mixture in 150 ml of saturated ammonia was treated with a solution of 30 g of barium chloride in 120 ml of water. The precipitate was filtered off and decomposed with hydrochloric acid. The product was percolated with ether, the extract dried with magnesium sulfate and evaporated to give 18.4 g of a crystallizing oil which was recrystallized from n-hexane and ether. There was obtained 7.6 g of trans-acid (XI) with m.p. 54-55°.

The filtrate from the precipitated barium salts was evaporated to dryness and decomposed with hydrochloric acid. Working-up as above gave 6.8 g of crystals from which was isolated 3.9 g of cis-acid (XII) with m.p. 104-105° [19].

The mother liquors were combined and subjected again to fractionation via the barium salts. Three repetitions of the operations gave a total of 15.7 g of trans-acid (XI) with m.p. 54.5-55° (from ligroine).

Found %: C 60.88, 60.82; H 8.95, 9.02. $C_8H_{14}O_3$. Calculated %: 60.72; H 8.92.

There was also isolated 5.5 g of cis-acid (XII) with m.p. 104.5-105° (from a mixture of ligroine and ether).

Found %: C 60.67, 60.60; H 8.72, 8.72. $C_8H_{14}O_3$. Calculated %: C 60.72; H 8.92.

The unresolvable residue amounted to 2 g.

Methylation of mixture of acids (XI) and (XII). An ethereal solution of diazomethane was added to an ethereal solution of the mixture of (XI) and (XII) until the color ceased to disappear. The mixture was left for 2 hr at 20°, after which it was dried with sodium sulfate and distilled to give 4.3 g of a mixture of methyl esters (XIII) and (XVI) with b.p. 71-75° (3 mm), $n^{20}D$ 1.4600.

Methylation of trans-acid (XI). To a solution of 15.2 g of trans-acid (XI) (m.p. 54-55°) in 60 ml of ether was added 340 ml of an ethereal solution of diazomethane (from 24 g of nitrosomethylurea), and the mass was worked up as described above. There was obtained 15.5 g of methyl ester of trans-3-methylcyclohexanol-carboxylic acid (XIII).

B. p. 80-80.5° (4 mm), $n^{20}D$ 1.4614, d^{20}_4 1.055, MR_D 44.76; calculated 44.74.

Found %: C 63.02, 62.84; H 9.45, 9.51. $C_9H_{16}O_3$. Calculated %: C 62.74; H 9.37.

Methylation of cis-acid (XII). By the preceding procedure, starting from 7.2 g of (XII) (m.p. 104-105°), there was obtained 6.8 g of methyl ester of cis-3-methylcyclohexanolcarboxylic acid (XVI).

B.p. 72-72.5° (4 mm), $n^{20}D$ 1.4556, d^{20}_4 1.044, MR_D 44.74; calculated 44.74.

Found %: C 62.57, 62.49; H 9.33, 9.28. $C_9H_{16}O_3$. Calculated % C 62.74; H 9.37.

Reduction of trans-ester (XIII). To a suspension of 5.4 g of lithium aluminum hydride in 250 ml of ether was added a solution of 12.1 g of trans-ester (XIII) in 50 ml of ether. When the thermal effect had ceased, the mixture was boiled for another 16 hr and treated with 20 ml of ethyl acetate and (with cooling) with dilute sulfuric acid. Neutralization was then effected with solid sodium bicarbonate. Working-up in the usual manner and distillation gave 9.2 g of trans-1-hydroxymethyl-3-methylcyclohexanol (XIV).

B.p. 103.5-104° (4 mm), $n^{20}D$ 1.4790.

Found %: C 66.69, 66.52; H 10.90, 11.01. $C_8H_{16}O_2$. Calculated % C 66.60; H 11.19.

Reduction of cis-ester (XVI). The ester (7.5 g) was reduced with 3.8 g of lithium aluminum hydride by the above procedure. Removal of the ether left 6.2 g of cis-1-hydroxymethyl-3-methylcyclohexanol (XVII) with m.p. 72-73° (from ligroine).

Found % C 66.69, 66.47; H 11.00, 11.00. $C_8H_{16}O_2$. Calculated % C 66.60; H 11.19.

Preparation and reduction of trans-tosylate (XV). A solution of 8.8 g of trans-diol (XIV) in 60 ml of anhydrous pyridine was cooled to 0° and portionwise addition was made of 13.5 g of p-toluenesulfochloride. The mixture was left for 48 hours at -3 to -4° and then worked up as described for the triol. Removal of the ether left 14 g of oil (XV), of which 12 g was dissolved in 75 ml of benzene and added to a suspension of 4.56 g of lithium aluminum hydride in 150 ml of ether and 75 ml of benzene. The temperature rose spontaneously to 42°. After heat had ceased to be liberated, the mixture was boiled for 20 hr and worked up in the usual manner. Distillation gave 3.2 g of trans-1,3-dimethylcyclohexanol (III), b.p. 78.5-79° (21 mm), $n^{20}D$ 1.4594, m.p. 26.5-27.5°, and 1.8 g of diol (XIV), b.p. 103-105° (4 mm), $n^{20}D$ 1.4792.

Boiling of trans-alcohol (III) with 3,5-dinitrobenzoyl chloride in pyridine gave the 3,5-dinitrobenzoate with m.p. 59.5-61° (from ligroine).

Preparation and reduction of cis-tosylate (XVIII). Starting from 5.6 g of cis-diol (XVII) in 43 ml of g anhydrous pyridine and 9.5 g of p-toluenesulfochloride, there was obtained by the above procedure 12.1 g of tosylate (XVIII) in the form of an oil. Reduction of 11 g by 4.4 g of lithium aluminum hydride (boiling for 21 hr) gave 3.1 g of cis-1,3-dimethylcyclohexanol (IV), b.p. 72-72.5° (21 mm), $n^{20}D$ 1.4527, m.p. 14-15°.

3,5-Dinitrobenzoate: m.p. 118.5-119° (from ligroine).

Preparation and separation of mixture of trans- and cis-alcohols (III) and (IV). To the Grignard reagent prepared from 17.5 g of magnesium and 99.4 g of methyl iodide in 250 ml of ether was added 56 g of 3-methylcyclohexanone (II) in 50 ml of ether. After completion of the addition, the mixture was boiled for 1 hr, treated with dilute hydrochloric acid, neutralized with solid sodium bicarbonate, and extracted three times with ether. The product was dried with magnesium sulfate and distilled to give 57.6 g of a mixture of trans- and cis-1,3-dimethylcyclohexanols (III) and(IV) with b.p. 65-69° (14 mm), $n^{20}D$ 1.4550.

With addition of 10 ml of the original ketone (II) and 15 ml of the high-boiling n-octyl alcohol, 50 ml of the above mixture was fractionated in a 35-plate column containing glass packing elements. The distillation curve shows that the mixture contains 40% of trans-alcohol (III) and 60% of cis-alcohol (IV).

Fractionation yielded 13.5 ml of cis-1,3-dimethylcyclohexanol (IV) with b.p. 70° (19 mm), $n^{20}D$ 1.4530, m.p. 14-15°.

Found %: C 74.79, 74.79; H 12.41, 12.31. $C_8H_{16}O$. Calculated %: C 74.92; H 12.50.

In addition we isolated 5 ml of trans-1,3-dimethylcyclohexanol (III), b.p. 76.5° (19 mm), $n^{20}D$ 1.4595, m.p. 25-27°.

Found %: C 74.73, 74.60; H 12.61, 12.40. $C_8H_{16}O$. Calculated %: C 74.92; H 12.50.

The 3,5-dinitrobenzoate of the cis-alcohol (IV) had m.p. 118-119° (from ligroine).

Found %: C 55.61, 55.68; H 5.57, 5.67; N 8.86, 8.72. $C_{15}H_{18}O_6N_2$. Calculated %: C 55.88; H 5.63; N 8.70.

The 3,5-dinitrobenzoate of the trans-alcohol (III) had m.p. 59.5-61° (from ligroine).

Found% : C 55.84; 55.84; H 5.72, 5.56,; N 8.74 8.71. $C_{15}H_{18}O_6N_2$. Calculated %: C 55.88; H 5.63; N 8.70.

A mixture of the 3,5-dinitrobenzoates of alcohols (III) and (IV) had m.p. 53-60°.

Literature data [12]: cis-alcohol (IV) m.p. 14.5°, b.p. 77.55° (25 mm), n^{20}_{5015} 1.4531, d^{30}_4 0.8893; trans-alcohol (III), m.p. 27.5°, b.p. 84.00° (25 mm), n^{20}_{5015} 1.4599, d^{30}_4 0.9021.

SUMMARY

1. A study was made of the stereochemistry of the addition of hydrocyanic acid and methylmagnexium iodide to 3-methylcyclohexanone and proof was obtained of the configuration of the resulting 1-cyano-3-methylcyclohexanols and 1,3-dimethylcyclohexanols and their derivatives (hydroxyacids, diols, etc.).

2. The results obtained are compared with those of an examination of the stereochemistry of addition reactions of 2-methylcyclohexanone.

3. Suggestions are made as to the roles of the polar orientation factors and steric hindrance in governing the steric directivity of the reactions investigated.

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TERTIARY TRIHYDRIC ALCOHOLS OF THE ACETYLENIC SERIES AND THEIR TRANSFORMATIONS

XVIII. OXIDATION BY POTASSIUM PERMANGANATE OF TRIOLS OF THE ACETYLENIC AND OLEFINIC SERIES

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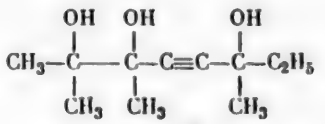
In our earlier publications on oxidation of triols of the acetylenic [1] and olefinic [2] series it was shown that when unsaturated hydroxyl-containing compounds are oxidized by potassium permanganate, cleavage does not inevitably occur at the multiple bond as might have been assumed on the basis of classical concepts of oxidation of unsaturated hydrocarbons. Oxidative cleavage of acetylenic and olefinic triols can occur both at multiple and at single bonds adjacent to a multiple bond; olefinic triols are cleaved to a large extent at single bonds with formation of a relatively large amount of oxalic acid. Oxidation of acetylenic triols proceeds mainly with cleavage at the triple bond to give a relatively larger amount of hydroxyacids. The fact that more oxalic acid is formed by oxidation of olefinic triols than by oxidation of acetylenic triols is a consequence of some special features of the mechanism of oxidation of these two classes of triols. We have previously discussed these features in detail [1, 2].

The objective of the present work was to confirm the correctness of the ideas advanced. Using aqueous potassium permanganate, we oxidized four acetylenic triols [3] (listed in table) and the corresponding four olefinic triols [4].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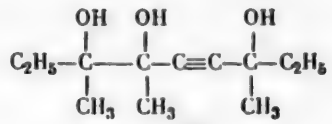
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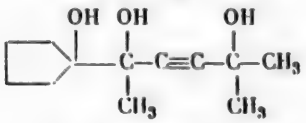
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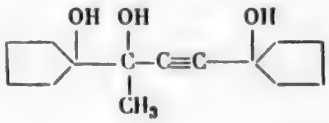
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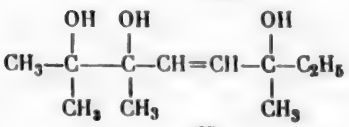
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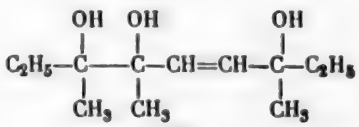
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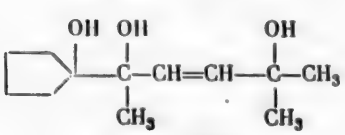
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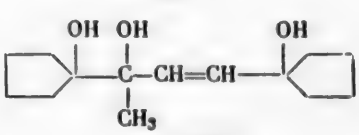
(VIII)

Compound No.	Oxidation product	Quantity of substance oxidized (g)	α-Hydroxyacids obtained		Amount of oxalic acid	
			in g	moles/mole of oxidized substance	in g	moles/mole of oxidized substance
	Tertiary acetylenic triols					
(I)	2,3,6-Trimethyloctyne-4-triol-2,3,6	15.3	5.1	0.56	3.8	0.39
(II)	3,4,7-Trimethylnonyne-5-triol-3,4,7	16.8	4.9	0.53	3.7	0.37
(III)	2-Methyl-5-(1-hydroxycyclopentyl)hexyne-3-diol-2,5	14.7	3.4	0.47	1.8	0.21
(IV)	2,4-Di-(1-hydroxycyclopentyl)-butyne-3-ol-2	10.1	3.4	0.62	1.3	0.24
	Tertiary olefinic triols					
(V)	2,3,6-Trimethyloctene-4-triol-2,3,6	5.6	0.35	1.101	1.3	0.515
(VI)	3,4,7-Trimethylnonene-5-triol-3,4,7	5.3	1.1	0.38	1.4	0.63
(VII)	2-Methy-5-(1-hydroxycyclopentyl) hexen-3-diol-2,5	4.7	Traces	Traces	1.3	0.657
(VIII)	2,4-Di-(1-hydroxycyclopentyl)-buten-3-ol-2	5.1	Traces	Traces	0.85	0.44

The products of oxidation of acetylenic triols support our earlier hypothesis.

Oxidation of (I), for example, gave methylethyl ketone, dimethylacetylcarbinol and acetic, oxalic, α-methyl-α-hydroxybutyric acids, and a minute amount of formic acid; oxidation of (II) gave methylethyl ketone, methylethylacetylcarbinol, and formic, acetic, oxalic and α-methyl-α-hydroxybutyric acid; oxidation of (III) gave acetone, cyclopentanone, acetylcyclopentanol, acetic, oxalic and α-hydroxyisobutyric acid, and a trace of formic acid. Oxidation of (IV) gave cyclopentanone, acetylcyclopentanol, and acetic, oxalic and cyclopentanol-1-carboxylic acids.

Triols of the olefinic series (V), (VI), (VII) and (VIII) gave on oxidation the same products as the acetylenic triols but, as we see from the table, in the former case the hydroxyacids predominate, whereas in the latter the oxalic acid predominates.

All these facts combine to confirm our earlier oxidation mechanism [1, 2].

EXPERIMENTAL

Oxidation of Tertiary Acetylenic Triols

Oxidation of 2,3,6-trimethyloctyne-4-triol-2,3,6 (I). A solution of 20 g of freshly distilled acetylenic triol (b.p. 121-122° at 1.5-2 mm) [3] in 100 ml of water was put into a flask fitted with a mechanical stirrer. This was followed by slow, dropwise addition (in 5 hr) of 1053 ml of 3% potassium permanganate solution (calculated for 3 active oxygen atoms per molecule of alcohol). Oxidation proceeded at room temperature. On the following day the transparent solution was filtered from manganese dioxide and the latter was washed several times with hot water. Steam-volatile neutral products were distilled off from the filtrate and 4.7 g of the original triol (I) was extracted from the residual solution of salts with ether. From the distillate was distilled off about 200 ml of the more volatile products. The distillate was salted out with ammonium sulfate and the following fractions collected by rectification in a 22-plate column: 1st, b.p. 69-73°, $n^{20}D$ 1.3832, 1.5 g; 2nd, b.p. 73-82°, 2.6 g.

From the first fraction was obtained methylethyl ketone 2,4-dinitrophenylhydrazone with m.p. 113-114°, which did not give a depression in admixture with the 2,4-dinitrophenylhydrazone of the authentic ketone.

The volatile neutral products were distilled off from the remaining distillate, and the residue saturated with ammonium sulfate and extracted with ether. From the ethereal extract was obtained 3.1 g of a substance which was fractionated at normal pressure and gave two fractions: 1st, b.p. to 135°, 0.9 g; 2nd, b.p. 135-136°, 1.3 g, $n^{20}D$ 1.4158; residue in flask 0.6 g.

From the 2nd fraction was isolated the semicarbazone of dimethylacetylcarbinol with m.p. 160-161°; no depression of melting point in a mixed test with authentic dimethylacetylcarbinol.

The solution of the salts was acidified with hydrochloric acid, and then the volatile acids were distilled off with steam. Neutralization of the volatile acids consumed 0.7593 g of sodium hydroxide. A trace of formic acid in the volatile acids was detected by the calomel formation test; acetic acid was detected by the reaction for cacodyl oxide. Oxalic acid (3.8 g), m.p. 101-102°, was isolated as calcium oxalate from the solution of the nonvolatile acids after neutralization; no depression in a mixed melting point test. The filtrate from the calcium oxalate was acidified with hydrochloric acid and extracted with ether in an extraction apparatus. Removal of the ether left 5.1 g of liquid which quickly crystallized. After two recrystallizations from a mixture (1 : 1) of ligroine and benzene, the crystals melted at 71-72° and consisted of α-methyl-α-hydroxybutyric acid [5].

Found %: C 51.34; H 8.82. M 116.6 [titration with $Ba(OH)_2$]. $C_5H_{10}O_2$. Calculated %: C 50.85; H 8.47. M 118.

The barium salt of this acid was prepared.

Found %: Ba 36.23. $(C_5H_8O_2)_2Ba$. Calculated %: Ba 36.99.

Products isolated after oxidation of 2,3,6-trimethyloctyne-4-triol-2,3,6 were therefore methylethyl ketone, dimethylacetylcarbinol, and acetic, oxalic, and α-methyl-α-hydroxybutyric acids in addition to a trace of formic acid.

Oxidation of 3,4,7-trimethylnonyne-5-triol-3,4,7 (II). Oxidation of 21 g of triol (b.p. 124-126° at 2 mm) [3] was effected in the above manner with 1030 ml of 3% potassium permanganate solution. The oxidation products were worked up by the above procedure. The amount of unoxidized triol recovered was 4.2 g.

Extraction of the distillate of neutral products with ether gave 5.5 g of products which were fractionated at normal pressure into four fractions: 1st, b.p. to 70°, 0.7 g; 2nd, b.p. 70-110°, 0.6 g; 3rd, b.p. 110-146°, 2.4 g; 4th, b.p. 146-148°, 1.3 g, $n^{20}D$ 1.4216; residue in flask 0.4 g. From the 2nd fraction was obtained a 2,4-dinitrophenylhydrazone with m.p. 113-114° (no depression in admixture with the 2,4-dinitrophenylhydrazone of methylethyl ketone). The 3rd fraction was an intermediate one. The 4th fraction was methylethylacetylcarbinol; it gave a semicarbazone with m.p. 150-151° which did not exhibit a depression of melting point in admixture with methylethylacetylcarbinol semicarbazone.

Neutralization of the distillate containing the volatile acids consumed 1.025 g of sodium hydroxide. Formic and acetic acids were detected by qualitative tests. From the nonvolatile acids were separated 3.7 g of oxalic acid with m.p. 101-102° and 4.9 g of α-methyl-α-hydroxybutyric acid—small white, transparent needles with m.p. 71-72°.

Consequently, the oxidation of 3,4,7-trimethylnonyne-5-triol-3,4,7 gave methylethyl ketone, methylethylacetylcarbinol and acetic, formic, oxalic and α-methyl-α-hydroxybutyric acids.

Oxidation of 2-methyl-5-(1-hydroxycyclopentyl)hexyne-3-diol-2,5 (III). Into a solution of 18 g of triol (m.p. 68-69°) [3] in 150 ml of water was slowly stirred 770 ml of 3% potassium permanganate solution. Isolation and examination of the oxidation products were carried out as in the first experiment. The amount of recovered triol was 3.3 g.

Rectification of the first portions of distillate of neutral products in a column yielded a fraction with b.p. 55-60° (0.4 g) from which was obtained a 2,4-dinitrophenylhydrazone with m.p. 124-126° (no depression in a mixed melting test with acetone 2,4-dinitrophenylhydrazone).

From the remaining distillate containing neutral products was isolated 3.6 g of a substance that distilled at normal pressure and gave the following fractions: 1st, b.p. 85-110°, 0.5 g; 2nd, b.p. 110-150°, 0.8 g; 3rd, b.p. 150-178°, 1.2 g; residue in flask 0.6 g. From the 2nd fraction was obtained a 2,4-dinitrophenylhydrazone with m.p. (after several recrystallizations from alcohol) of 144-145° (no depression in mixed melting test with the 2,4-dinitrophenylhydrazone of cyclopentanone). From the 3rd fraction was obtained a semicarbazone with m.p. 188-189° (no depression in a mixed melting test in admixture with the semicarbazone of an authentic specimen of acetylcyclopentanol).

The distillate fraction containing the volatile acids was neutralized with 0.4092 g of sodium hydroxide. Acetic and formic acids were detected by qualitative tests (the calomel precipitate was very small). From the nonvolatile acids were isolated 1.8 g of oxalic acid with m.p. 101-102° (mixed melting test) and 3.4 g of a liquid which crystallized; m.p. 79° (from benzene) (no depression in a mized melting test with α-hydroxyisobutyric acid).

Consequently the oxidation of 2-methyl-5-(1-hydroxycyclopentyl)hexyne-3-diol-2,5 gave acetone, cyclopentanone, acetylcyclopentanol, acetic, oxalic and α-hydroxyisobutyric acids, and a trace of formic acid.

Oxidation of 2,4-di-(1-hydroxycyclopentyl)butyn-3-ol-2 (IV). Oxidation of 13 g of the acetylenic triol (m.p. 93-94°) [3] was effected with 500 ml of 3% potassium permanganate solution. Oxidation products were isolated and examined as before. The amount of 2,4-di-(1-hydroxycyclopentyl)-butyn-3-ol recovered unchanged was 2.9 g.

From the distillate was obtained 2.8 g of neutral products which were fractionated at normal pressure to give the following fractions: 1st, b.p. 80-130°, 0.6 g; 2nd, b.p. 130-160°, 0.4 g; 3rd, b.p. 160-172°, 1.1 g; residue in flask 0.4 g.

The first fraction was mainly cyclopentanone; it gave a 2,4-dinitrophenylhydrazone with m.p. 145-146° (no depression in a mixed melting test with the 2,4-dinitrophenylhydrazone of authentic cyclopentanone); the 3rd fraction formed a semicarbazone with m.p. 188-189° (no depression in a mixed melting test with the semicarbazone of acetylcyclopentanol).

The distillate containing the volatile acids was neutralized by 0.084 g of sodium hydroxide. Acetic acid was detected by a qualitative test. Formic acid was not detected. From the nonvolatile acids were collected 1.3 g of oxalic acid with m.p. 101-102° (mixed melting test) and 3.4 g of a liquid from which fine crystals came out; the latter were freed of liquid on a porous tile and recrystallized from a 1 : 1 mixture of ligroine and benzene; m.p. 102-103°; identical with cyclopentanol-1-carboxylic acid [6].

Found %: C 55.75; H 7.89. M 130.5. [titration with $Ba(OH)_2$]. $C_6H_{10}O_3$. Calculated %: C 55.38; H 7.69. M 130.

The barium salt of this acid was prepared.

Found %: Ba 34.06. $(C_6H_9O_3)_2$ Ba. Calculated %: Ba 34.74.

Consequently, the oxidation of 2,4-di-(1-hydroxycyclopentyl)butyn-3-ol-1 gave cyclopentanone, acetylcyclopentanol and acetic, oxalic and cyclopentanol-1-carboxylic acids.

Oxidation of Tertiary Olefinic Triols

Oxidation of 2,3,6-trimethyloctene-4-triol-2,3,6 (V). Into a mixture of 7 g of triol (b.p. 114-115° at 2 mm)[4], 70 ml of water and 1 g of potassium carbonate in a flask was slowly stirred (mechanically) 607 ml of 3% potassium permanganate solution (the amount of oxidant corresponded to 5 active oxygen atoms per mole of triol). Oxidation was performed at 17° for 3 days since the triol was sparingly soluble in water. Reaction products were worked up in the same way as those of acetylenic triols. Unoxidized triol was recovered in the amount of 1.4 g.

From the neutral products were isolated the following fractions: 1st, b.p. 55-58°; 2nd, b.p. 71-75°; the first fraction formed a 2,4-dinitrophenylhydrazone with m.p. 123° (from alcohol), identified (mixed melting test) as the 2,4-dinitrophenylhydrazone of acetone. From the 2nd fraction was isolated a 2,4-dinitrophenylhydrazone with m.p. 111-112°, identified in a mixed melting test as the 2,4-dinitrophenylhydrazone of methylethyl ketone. No other neutral products were isolated.

Neutralization of the volatile acids consumed 0.8495 g of sodium hydroxide. Acetic and formic acids were detected by qualitative tests. The total analysis of the silver salts indicated a small content of formic acid.

Found %: Ag 65.00. $C_2H_3O_2Ag$. Calculated %: Ag 64.67. CHO_2Ag. Calculated %: Ag 70.5.

From the nonvolatile acids were obtained 1.3 g of oxalic acid with m.p. 101-102° (mixed melting test) and 0.35 g of α-methyl-α-hydroxybutyric acid with m.p. 71-72° (mixed melting test).

Consequently the oxidation of 2,3,6-trimethyloctene-4-triol-2,3,6 gave acetone, methylethyl ketone, and acetic, oxalic and α-methyl-α-hydroxyisobutyric acids, also a trace of formic acid.

Oxidation of 3,4,7-trimethylnonene-5-triol-3,4,7 (VI). Oxidation of 7 g of the triol (b.p. 126-127° at 2 mm) [4] in 70 ml of water was effected in presence of 2 g of potassium carbonate with 571 ml of 3% potassium permanganate solution by the above procedure. Oxidation was carried out at 16° for 2 days. The products were worked up as in the case described above. The amount of unoxidized substance recovered was 1.7 g.

Two fractions were collected from the neutral distillate in a 22-plate column: 1st, b.p. 70-75°; 2nd, b.p. 75-80°. From these fractions was isolated a 2,4-dinitrophenylhydrazone which in both cases melted at 112° (from alcohol) and was identical with the 2,4-dinitrophenylhydrazone of methylethyl ketone (mixed melting point test). No other neutral products were isolated.

The distillate containing the volatile acids was neutralized with 0.7061 g of sodium hydroxide. Acetic and formic acids were detected by qualitative tests, and silver acetate was formed.

Found %: Ag 64.80. $C_2H_3O_2Ag$. Calculated %: Ag 64.67. CHO_2Ag. Calculated%: Ag 70.50.

From the nonvolatile acids were isolated 1.4 g of oxalic acid with m.p. 101-102° (mixed melting point test) and 1.1 g of α-methyl-α-hydroxybutyric acid with m.p. 71-72° (mixed melting point test).

Oxidation of 3,4,7-trimethylnonene-5-triol-3,4,7 thus gave methylethyl ketone and the following acids: formic (trace), acetic, oxalic and α-methyl-α-hydroxybutyric.

Oxidation of 2-methyl-5-(1-hydroxycyclopentyl)hexene-3-diol-2,5 (VII). Oxidation of 5.5 g of triol with m.p. 113-114° [4] was carried out for several days at 16-17° in 70 ml of water and in the presence of 1 g of potassium carbonate. The oxidizing agent was 451 ml of 3% potassium permanganate solution. The amount of unreacted starting substance was 0.8 g.

A fraction with b.p. 55-60° was collected at normal pressure in a column from the distillate containing the neutral products. From this fraction was obtained acetone 2,4-dinitrophenylhydrazone with m.p. 123° (mixed melting point test). The same distillate also yielded a fraction boiling at normal pressure at 124-135°. This fraction gave a 2,4-dinitrophenylhydrazone with m.p. 144-145° which was identical with the 2,4-dinitrophenylhydrazone of cyclopentanone (mixed melting point test). No other neutral products were collected.

Neutralization of the volatile acids consumed 0.253 g of sodium hydroxide. Acetic acid was detected in the distillate from the volatile acids by the cacodyl test; a minor amount of formic acid was detected by calomel formation.

Found %: Ag 65.20. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids was isolated 1.3 g of oxalic acid with m.p. 101-102° (mixed melting point test), as well as a trace of α-hydroxyisobutyric acid with m.p. 78-79° (mixed melting point test).

Oxidation of 2-methyl-5-(1-hydroxycyclopentyl)hexene-3-diol-2,5 thus gave acetone, cyclopentanone, and acetic, formic, oxalic and α-hydroxyisobutyric acid.

Oxidation of 2,4-di-(1-hydroxycyclopentyl)buten-3-ol-2 (VIII). In presence of 1 g of potassium carbonate in 70 ml of water, 7 g of the olefinic triol (m.p. 129-130° [4]) was oxidized with 511 ml of 3% potassium permanganate solution at 20° for 4 days. The amount of unoxidized triol recovered was 1.9 g.

From the neutral products was isolated a fraction of 0.3 g with b.p. 125-130° (normal pressure). This fraction gave a 2,4-dinitrophenylhydrazone with m.p. 145-146° (from alcohol) which was identical with the 2,4-dinitrophenylhydrazone of cyclopentanone (mixed melting test). No other neutral products were isolated.

Neutralization of the volatile acids consumed 0.1282 g of sodium hydroxide. Acetic and formic acids were detected by the cacodyl test and by calomel formation, respectively.

Analysis of silver salt: Found %: Ag 65.00. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids was obtained 0.85 g of oxalic acid with m.p. 101-102° (mixed melting point test). After the calcium oxalate had been separated, the solution of the salts was acidified with hydrochloric acid and treated with ether in an extraction apparatus for 20-25 hr. Removal of the ether from the extract left an insignificant amount of crystals which were recrystallized with difficulty from a mixture of ligroine and benzene; m.p. 102-103°; identified as cyclopentanol-1-carboxylic acid (mixed melting point test). Authentic cyclopentanol-1-carboxylic acid was prepared by oxidation of ethynylcyclopentanol.

Oxidation of 2,4-di-(1-hydroxycyclopentyl)buten-3-ol-2 thus gave cyclopentanone and acetic, formic (trace), oxalic and cyclopentanol-1-carboxylic acids.

SUMMARY

Confirmation is obtained for the mechanism earlier proposed for the oxidation of hydroxyl-containing compounds of the acetylenic and olefinic series whose hydroxyl groups are at carbons adjacent to carbons to which the multiple bonds are attached.

Acetylenic hydroxyl-containing derivatives are oxidized predominantly with rupture at the triple bond. Oxidation of olefinic hydroxyl compounds proceeds mainly at the single bonds adjacent to the double bond.

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•Original Russian pagination. See C. B. Translation.

••See English translation.

TERTIARY TRIHYDRIC ALCOHOLS OF THE ACETYLENIC SERIES AND THEIR TRANSFORMATIONS

XIX. OXIDATION OF SUBSTITUTED DIHYDRO-5-PYRANOLS

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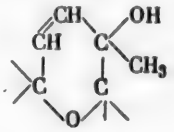
In earlier work on oxidation by potassium permanganate of triols of the acetylenic [1, 2] and olefinic [2, 3] series, it was shown that oxidative cleavage of olefinic triols at the double bond occurs to a lesser extent than cleavage of acetylenic triols at the triple bond. This is reflected in a higher content of oxalic acid than of hydroxyacids in the end product.

We previously prepared substituted dihydro-5-pyranols of general formula A by hydrogenation of acetylenic triols to olefinic triols [4] and dehydration of the latter [5].



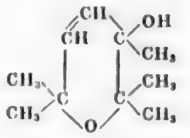
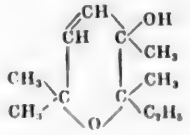
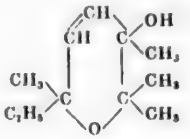
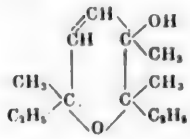
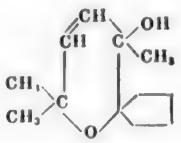
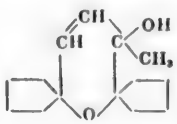
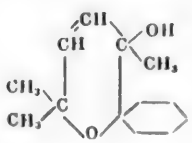
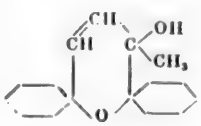
(A)

The primary objective of the present work was to elucidate the behavior of the double bond in the above dihydropyranols in presence of potassium permanganate solution. The following eight representatives of substituted dihydropyranols containing methyl, ethyl, cyclopentyl and cyclohexyl radicals were subjected to oxidation: 2,2,5,6,6-pentamethyldihydro-5-pyranol (I); 2,2,5,6-tetramethyl-6 ethyldihydro-5-pyranol (II); 2,5,6,6-tetramethyl-2-ethyldihydro-5-pyranol (III); 2,5,6-trimethyl-2,6-diethyldihydro-5-pyranol (IV); 2,2,5-trimethyl-6-spirocyclopentanedihydro-5-pyranol (V); 5-methyl-2,6-dispirocyclopentanedihydro-5-pyranol (VI); 2,2,5-trimethyl-6-spirocyclohexanedihydro-5-pyranol (VIII); 5-methyl-2,6-dispirocyclohexanedihydro-5-pyranol (VIII).

Results are summarized in the table. The amount of acids formed is expressed as moles per mole of oxidized substance. Permanganate oxidation of dihydropyranols is seen to follow the same law as oxidation of olefinic triols: Cleavage occurs predominantly not at the double bond but at the "ends" of this bond with formation of oxalic acid. The reaction evidently proceeds via glycoaldehyde. Hydroxyacids, which must have been formed by cleavage at the double bond, were obtained in quantities 5, 10 or even 25 times smaller than the yield of oxalic acid. In some cases only traces of hydroxyacids were formed.

EXPERIMENTAL

Oxidation of 2,2,5,6,6-pentamethyldihydro-5-pyranol (I). To 3 g of (I) (b.p. 61-62° at 8 mm), 25 ml of water and 0.5 g of potassium carbonate was slowly added 310 ml of 3% potassium permanganate solution (amount calculated for 5 active oxygen atoms per mole of starting compound). Oxidation was conducted at room temperature and the reaction products were worked up in the usual manner. Oxidation was complete. From the distillate

Compound No.	Formula	Amount of substance oxidized		Amount obtained of hydroxy-acids		Amount obtained of oxalic acid		NaOH consumed for neutralization of volatile acids	
		(in g)	(in moles per mole of substance oxidized)	(in g)	(in moles per mole of substance oxidized)	(in g)	(in moles per mole of substance oxidized)	(in moles)	(in moles per mole of substance oxidized)
(I)		3.0	0.0176	Traces		0.4	0.25	0.009	0.51
(II)		9.2	0.05	Traces		2.0	0.44	0.029	0.58
(III)		9.8	0.05	0.75	0.12	2.5	0.52	0.049	0.98
(IV)		4.2	0.02	0.05	0.02	1.0	0.52	0.02	1.0
(V)		10.1	0.051	0.1	0.017	2.3	0.5	0.011	0.2
(VI)		5.5	0.025	—		0.65	0.28	0.0033	0.13
(VII)		8.0	0.038	0.2	0.052	2.2	0.63	0.023	0.61
(VIII)		5.9	0.02	Traces		1.9	0.7	0.0175	0.87

of neutral products was collected (in a column) a 54-55° fraction (normal pressure). From this fraction was obtained acetone 2,4-dinitrophenylhydrazone with m.p. 123° (from methanol), identified by a mixed melting test. No other neutral products were isolated.

Neutralization of the volatile acids consumed 0.3612 g of sodium hydroxide. In the volatile-acid distillate were qualitatively detected insignificant traces of formic acid (calomel formation test) and acetic acid (cacodyl test).

Silver salt analysis: Found %: Ag 63.30, 63.90. CH_3COOAg. Calculated %: Ag 64.67.

The low result in the analysis of the silver salt indicates the presence of a little α-hydroxyisobutyric acid in the volatile acids. From the neutralized solution remaining after removal of the volatile acids was isolated (via calcium oxalate) 0.4 g of oxalic acid with m.p. 101-102° (mixed melting point test). The filtrate from the calcium oxalate, containing salts of other acids, was acidified with hydrochloric acid and treated with ether in an extraction apparatus for 25-30 hr. Removal of the ether left a very minute amount of what was apparently α-hydroxyisobutyric acid.

Oxidation of dihydropyranol (I) thus gave acetone, traces of formic, acetic and oxalic acids, and possibly also of α-hydroxyisobutyric acid.

Oxidation of 2,2,5,6-tetramethyl-6-ethyldihydro-5-pyranol (II). Into a flask were charged 9.2 g of (II) (b.p. 70-72° at 8 mm), 75 ml of water, 1 g of potassium carbonate and 890 ml of 3% potassium permanganate solution (amount calculated for 5 active oxygen atoms). Oxidation was conducted at 10° and the products were worked up as in previous cases. Oxidation was complete. Distillation of neutral products in a rectifying column gave two fractions: 1st, b.p. 52-55°; 2nd, b.p. 71-80°. The first fraction gave acetone 2,4-dinitrophenylhydrazone with m.p. 123° (from methanol), identified in mixed melting test. The second fraction gave methylethyl ketone 2,4-dinitrophenylhydrazone with m.p. 112-113° (from alcohol). Its mixture with the authentic 2,4-dinitrophenylhydrazone did not show a melting point depression. No other neutral products were isolated.

Neutralization of the volatile acids consumed 1.188 g of sodium hydroxide. Formic acid (trace) and acetic acid were detected in the volatile-acid distillate.

Found %: Ag 64.73, 64.41. $C_2H_7O_2Ag$. Calculated %: Ag 64.67.

Oxalic acid (2 g) was isolated via the calcium salt from the nonvolatile acids; m.p. 101-102° (mixed melting point test). Traces of (apparently) α-hydroxyisobutyric acid were also isolated.

Oxidation of dihydropyranol (II) thus gave acetone, methylethyl ketone, traces of formic, acetic and oxalic acid, and possibly also traces of α-hydroxyisobutyric acid.

Oxidation of 2,5,6,6-tetramethyl-2-ethyldihydro-5-pyranol (III). Into a flask were charged 9.8 g of (III) (b.p. 74.5° at 8 mm), 70 ml of water, 1 g of potassium carbonate and 933 ml of 3% potassium permanganate solution. Oxidation was conducted at 26° and 0.75 g of the compound was recovered (b.p. 73-74.5°, $n^{20}D$ 1.4562).

Three fractions were distilled off from the neutral products: 1st, b.p. 56-57°; 2nd, b.p. 66-71°; 3rd, b.p. 71-80°. From the 1st fraction was obtained acetone 2,4-dinitrophenylhydrazone with m.p. 122-123° (mixed melting test). The 2nd fraction was an intermediate one, judging by the m.p. of 91-101° of its 2,4-dinitrophenylhydrazone. The 3rd fraction gave methylethyl ketone 2,4-dinitrophenylhydrazone with m.p. 111-112° (mixed melting test).

Neutralization of the volatile acids consumed 1.966 g of sodium hydroxide. Acetic acid was detected qualitatively and by analysis of the silver salt.

Found %: Ag 64.82. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids was obtained 2.5 g of oxalic acid with m.p. 101-102° (mixed melting test). The filtrate from the calcium oxalate was acidified with hydrochloric acid and extracted with ether in an extraction apparatus for 24-30 hr. Removal of the ether left 0.75 g of crystals with m.p. 71-72° (from benzene); no depression of m.p. in admixture with authentic methylethylhydroxyacetic acid.

Oxidation of dihydropyranol (III) thus gave acetone, methylethyl ketone, and acetic, oxalic and methylethylhydroxyacetic acids.

Oxidation of 2,5,6-trimethyl-2,6-diethyldihydro-5-pyranol (IV). Oxidation of 4.2 g of (IV) (b.p. 90-91° at 8 mm) was effected in 70 ml of water, in presence of 1 g of potassium carbonate, with 372 ml of 3% potassium permanganate solution. Oxidation was carried out at 25° for 6 hr and 0.15 g of unoxidized substance was recovered.

A fraction (0.5 g) with b.p. 70-75° was taken off at normal pressure from the neutral products in a column. This was identified as methylethyl ketone through the 2,4-dinitrophenylhydrazone; m.p. 112° (from alcohol); no depression in mixed melting test. No other neutral products were isolated.

Neutralization of the distillate of volatile acids consumed 0.813 g of sodium hydroxide. Acetic acid and formic acid (traces) were detected by qualitative tests.

Found %: Ag 64.93. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids were isolated 1 g of oxalic acid with m.p. 101-102° (mixed melting test) and 0.05 g of methylethylhydroxyacetic acid with m.p. 71-72° (mixed melting test).

Oxidation of dihydropyranol (IV) thus gave methylethyl ketone, acetic, oxalic and α-methylethylhydroxyacetic acids, and a trace of formic acid.

Oxidation of 2,2,5-trimethyl-6-spirocyclopentanedihydro-5-pyranol (V). In a flask were placed 10.1 g of (V) (b.p. 98-99° at 8 mm, $n^{20}D$ 1.4820), 75 ml of water and 1 g of potassium carbonate, followed gradually by 903 ml of 3% potassium permanganate solution. Oxidation was conducted at 26-28°. Distillation of the neutral products in a 22-plate column gave a 64-65° fraction from which acetone 2,4-dinitrophenylhydrazone was obtained with m.p. 122-123° (mixed melting test). A second fraction boiled at 150-168° (normal pressure) and gave a semicarbazone identified as that of acetylcyclopentanol, m.p. 187-188°. No other neutral oxidation products were isolated.

Neutralization of the volatile acids consumed 0.4376 g of sodium hydroxide. The acid distillate contained acetic acid and traces of formic acid.

Analysis of silver salt: Found %: Ag 64.96. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids were isolated (by the previous procedure) 2.3 g of oxalic acid with m.p. 101-102° (mixed melting test) and 0.1 g of α-hydroxyisobutyric acid with m.p. 78-79° (mixed melting test).

Oxidation of dihydropyranol (V) thus gave acetone, acetylcyclopentanol, acetic, formic, oxalic and α-hydroxyisobutyric acids, and traces of formic acid.

Oxidation of 5-methyl-2,6-dispirocyclopentanedihydro-5-pyranol (VI). In a flask were placed 6.3 g of (VI) (b.p. 126-126.5° at 8 mm, $n^{20}D$ 1.5030), 70 ml of water and 1 g of potassium carbonate, followed gradually by 513 ml of 3% potassium permanganate solution. Oxidation was performed at 27 °, and 0.8 g of unreacted substance was recovered ($n^{20}D$ 1.5028, b.p. 120-123° at 8 mm).

From the neutral products was distilled 0.3 g of a 145-146° fraction from which was derived cyclopentanone 2,4-dinitrophenylhydrazone, m.p. 145-146° (mixed melting test). No other neutral products were isolated.

Neutralization of the volatile acids consumed 0.1325 g of sodium hydroxide. Acetic and formic acids were detected in the distillate.

Analysis of the silver salt: Found %: Ag 65.20. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

Contamination with formic acid accounts for the too high value for silver in the silver acetate.

Oxalic acid (0.65 g) with m.p. 102-103° was separated from the nonvolatile acids by the usual method.

Oxidation of dihydropyranol (VI) thus gave cyclopentanone, acetic and oxalic acids, and traces of formic acid.

Oxidation of 2,2,5-trimethyl-6-spirocyclohexanedihydro-5-pyranol (VII). Components in the flask were 8 g of (VII) (b.p. 108-109° at 8 mm), 1 g of potassium carbonate and 680 ml of 3% potassium permanganate solution. Operating and working-up conditions were as in the previous cases.

Two fractions were taken off from the neutral products in a column at normal pressure: 1st, b.p. 55-56°; 2nd, b.p. 120-150°. From the first fraction was prepared acetone 2,4-dinitrophenylhydrazone with m.p. 123°; and from the second cyclohexanone semicarbazone with m.p. 165-166° (from methanol). No other neutral products were isolated.

Neutralization of the volatile acids consumed 0.9187 g of sodium hydroxide. Acetic acid was detected in the distillate.

Analysis of the silver salt gave low results, evidently due to contamination with α-hydroxyisobutyric acid.

Found %: Ag 62.60. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids were isolated oxalic acid (2.2 g), m.p. 101-102° (mixed melting test); α-hydroxyisobutyric acid (0.2 g), m.p. 79° (mixed melting test); and adipic acid (0.25 g), m.p. 152-153° (mixed melting test). The latter resulted from oxidation of cyclohexanone.

Oxidation of dihydropyranol (VII) thus gave acetone, cyclohexanone, and acetic, oxalic, α-hydroxyisobutyric and adipic acids.

Oxidation of 5-methyl-2,6-dispirocyclohexanedihydro-5-pyranol (VIII). To 6 g of (VIII) (b.p. 121-122° at 2 mm), 50 ml of water and 1 g of potassium hydroxide was added 430 ml of 3% potassium permanganate solution. One g of unoxidized substance was recovered.

A 100-150° fraction was taken off from the neutral products in a column. This gave a semicarbazone with m.p. 164-165° (from methanol), and identified as cyclohexanone semicarbazone (mixed melting test).

Neutralization of the volatile acids consumed 0.702 g of sodium hydroxide. The distillate contained acetic acid (characterized by the silver salt).

Found %: Ag 63.75, 63.90. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

From the nonvolatile acids was isolated (via the calcium salt) 1.3 g of oxalic acid with m.p. 101-102° (mixed melting test). In addition, as in the oxidation of 2,4-di-(1-hydroxycyclohexyl)butenol, a small quantity of α-hydroxyhexahydrobenzoic acid with m.p. 105-106° (mixed melting test) and adipic acid (0.9 g) with m.p. 152-153° (mixed melting test) were obtained.

Oxidation of dihydropyranol (VIII) thus gave cyclohexanone, and acetic, oxalic, α-hydroxyhexahydrobenzoic and adipic acids.

SUMMARY

Substituted dihydro-5-pyranols are oxidized by potassium permanganate by the mechanism applicable to triols of the olefinic series, i.e., with cleavage not at the double bond of the dihydropyran ring but mainly at the single bond adjacent to the double bond, with formation of oxalic acid.

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•Original Russian pagination. See C. B. Translation.

CYCLIC ACETALS OF OXYCARBONYL COMPOUNDS

X. METHYLLACTOLIDES OF DIMETHYL-p-ANISOYL- AND DIMETHYL-p-CHLOROBENZOYLCARBINOLS AND THEIR TRANSFORMATIONS

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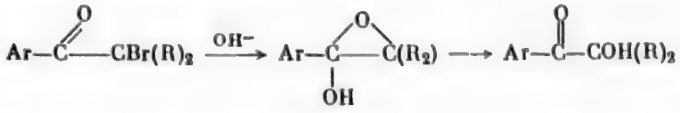
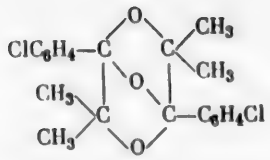
A large number of α-methoxyoxides have now been prepared; these are methyllactolides of α-ketoalcohols of the aromatic and aliphatic-aromatic series. The only representative containing a substituent in the benzene ring—the methyllactolide of methyl-p-anisoylcarbinol—was found to be so unstable that it could not be closely investigated [1]. In this work we attempted the synthesis of two methyllactolides of nuclear-substituted α-ketoalcohols containing substitutents in the para position differing in their electrochemical influence on the benzene ring—the methyllactolide of dimethyl-p-anisoylcarbinol (II, X = CH_3O) and the methyllactolide of dimethyl-p-chlorobenzoylcarbinol (II, X = Cl). Both compounds were fairly stable. Introduction into the para position of a methoxy group, which has a strong +C-effect, did not appreciably reduce the stability of this methoxyoxide in comparison with one not substituted in the ring; the methyllactolide is stable when fractionated at a relatively high temperature (150-160°). Both compounds can be kept in sealed ampoules for a long period without change, but they are extremely hygroscopic and rapidly hydrolyze to the corresponding α-ketoalcohols (III). This behavior is especially striking when a methoxyl is in the para position, so that careful exclusion of atmospheric moisture is essential for the preparation of the pure methyllactolide of dimethyl-p-anisoylcarbinol. This methyllactolide is a nicely crystallizing substance with m.p. 38.5-39°. Its weight very rapidly increases when kept in an atmosphere saturated with water vapor at room temperature, one mole of water being taken up per two moles of methoxyoxide. The weight then starts to fall, especially in a desiccator over $CaCl_2$, or on drying in vacuo, and the crystalline substance changes to a viscous oil. Under these conditions the methyllactolide of dimethyl-p-anisoylcarbinol changes into the ketoalcohol.

Dimethyl-p-chlorobenzoylcarbinol was prepared directly from α-bromoisopropyl-p-chlorophenyl ketone (I, X = Cl) in presence of alkali. The bromine in this bromoketone is very easily replaced by hydroxyl in the cold (the reaction is exothermic). This increased reaction rate when a chlorine atom is in the para position supports the theory [2] that replacement of bromine in bromoketones involves intermediate formation of an α-epoxide which immediately isomerizes to an α-ketoalcohol [3].

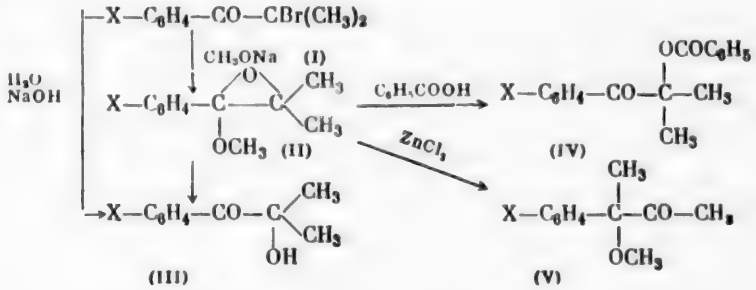


The α-ketoalcohol with a chlorine in the para position is extremely unstable in the free state, particularly in presence of acids, and it quickly changes into the anhydrodimer; the same rapid transformation occurs in alcoholic and ethereal solutions. The anhydrodimer is an analog of the substance previously obtained by A. E. Favorskii and N. Mandryko from dimethylbenzoylcarbinol [4]. It may have the tricyclic structure (VI).



(VI)

Treatment of methyllactolides with benzoic acid gives the benzoic esters of the corresponding α-keto-alcohols (IV); heating of methyllactolides in presence of $ZnCl_2$ gives the methyl ethers of the isomeric α-keto-alcohols (methoxyketones V).



EXPERIMENTAL •

I. Methyllactolide of Dimethyl-p-anisolcarbinol (II, X = CH_3O) ••

The starting substance—α-bromoisopropylanisyl ketone [5]—was obtained in the form of a light-green liquid with b.p. 138-139° at 4 mm or 146-147° at 5 mm, $n^{20}D$ 1.5712. In one experiment it was obtained in the crystalline form. The bromoketone is very unstable. For preparation of the methyllactolide the α-bromo-ketone was added to 4-5 times the quantity of sodium methoxide suspended in absolute ether. The reaction was slightly exothermic and was completed in 6-8 hr. The resulting oil was worked up in the usual manner and fractionated in vacuo before rectification in a column.

B. p. 84° at 2 mm, 92° at 3 mm, 97° at 4 mm, 108.5° at 6 mm; m.p. 38.5-39°; immediately after distillation (in the supercooled state) $n^{20}D$ 1.5035.

Found %: C 68.93, 68.97; H 7.87, 7.87; OCH_3 29.14, 29.14. $C_{12}H_{16}O_3$. Calculated %: C 69.2; H 7.75; OCH_3 29.84.

The infrared spectrum contains the frequencies (897 and 924 cm^{-1}) characteristic of the methoxyoxides of the aliphatic-aromatic series.

From the higher boiling fraction was isolated a substance with b.p. 133-137° at 3.5 mm, consisting of not perfectly pure ketoalcohol—dimethyl-p-anisoylcarbinol.

A fine orange precipitate came down when the methyllactolide was treated with 2,4-dinitrophenylhydrazine in aqueous alcoholic solution acidified with sulfuric acid. After recrystallization from alcohol, the dark-red crystals melted with decomposition at 135-140°. Brick-red crystals were unexpectedly obtained after one of the recrystallizations; m.p. 110-121°; from the mother liquor was obtained a substance with m.p. 139-143°. Identical compositions were found when both forms of crystals were analyzed for nitrogen.

M.p. 135-143°. Found %: N 15.05, 15.09. M.p. 110-121°. Found %: N 15.15, 15.09. $C_{17}H_{18}O_6N_4$. Calculated %: N 14.96.

Reaction of methyllactolide of dimethyl-p-anisoylcarbinol with benzoic acid. The reaction was carried out in benzene solution. The resulting benzoic ester of dimethyl-p-anisoylcarbinol (IV, X = CH_3O) was recrystallized from ligroine and melted at 73.5-74.5°.

• The experimental procedure is described in detail in preceding papers in this series.

••Experiment carried out by R. Gissel'.

Found %: C 72.26, 72.21; H 6.22, 6.27. $C_{18}H_{18}O_4$. Calculated %: C 72.46; H 6.08.

Dimethyl-p-anisoylcarbonyl (III, X = CH_3O) was prepared by hydrolysis of the bromoketone with aqueous NaOH at the boil for 3 hr or by hydrolysis of the methyllactolide with 5% sulfuric acid solution (also with heating). In both cases a substance with m.p. 54-55° (from gasoline) was obtained.

Found %: C 67.91, 67.98; H 7.22, 7.53. $C_{11}H_{14}O_3$. Calculated %: C 68.02; H 7.27.

The infrared spectrum contains a characteristic maximum at 1669 cm^{-1} (carbonyl group conjugated with phenyl).

Isomerization of methyllactolide of dimethyl-p-anisoylcarbinol to the methyl ester of methyl-p-anisylacetylcarbinol (V, X = CH_3O) was effected over $ZnCl_2$ by the procedure already described [6]. Yield of methoxyketone approximately 70%. A very pure product was obtained by the method of crystallization under equilibrium conditions followed by fractional fusion [7].

B.p. 102-103° at 2.5 mm, 107-108° at 3 mm, m.p. 41-42° (39-41° on the hot stage under a microscope).

Found %: C 69.07, 69.11; H 7.85, 7.90. $C_{12}H_{16}O_3$. Calculated %: C 69.20; H 7.75.

The infrared spectrum contains a strong band at 1716 cm^{-1}, corresponding to the valence vibration of the unconjugated carbonyl.

II. Methyllactolide of Dimethyl-p-chlorobenzoylcarbinol (II, X = Cl) •

Isopropyl-p-chlorophenylketone was prepared by a procedure similar to that employed for synthesis of p-chloroethylphenyl ketone [8]. To a suspension of finely pulverized $AlCl_3$ (220 g) in 700 ml of CS_2 was added (with good stirring and cooling) 180 g of isobutyryl chloride and 250 g of chlorobenzene. After 72-hr stirring in the cold, the reaction mixture was heated at 50-60° for 8 hr and cautiously poured onto ice. The ketone was purified by steam distillation. Yield approximately 50%.

The mixture of isomeric chloroketones (o- and p-) was fractionally distilled in vacuo. The main mass (approx. 95% of the total ketones) came over at 97-99° (4 mm), $n^{20}D$ 1.5349, $n^{25}D$ 1.5325.

The same chloroketones were prepared by condensation of chlorobenzoyl chlorides with ethyl α-bromoisobutyrate (Reformatskii reaction) and subsequent decomposition of the β-ketoacids [9]; the following constants were reported: o-chloroketone: b.p. 121-122° (17 mm), $n^{25}D$ 1.520; p-chloroketone: b.p. 142-143° (19 mm), $n^{23}D$ 1.534.

Since our ketone had a boiling point closer to the ortho isomer, while its refractive index was nearer that of the para isomer, we prepared the semicarbazone (m.p. 185-186°) which was identified as the derivative of the para isomer. Oxidation of the chloroketone with potassium permanganate gave p-chlorobenzoic acid with m.p. 242-243°. The preparation thus gave almost exclusively the para isomer of the ketone.

α-Bromoisopropyl-p-chlorophenyl ketone (I, X = Cl) was prepared by direct bromination of the ketone in CCl_4 solution. The reaction went with great facility, decolorization of the bromine starting immediately after addition of the first drops. The CCl_4 was removed from the reaction product in vacuo. The bromoketone was a colorless, rather mobile and odorless liquid, hardly irritating the muscous membranes of the eyes. Stable on keeping. Yield approximately 85%.

B.p. 123-124° at 4 mm, $n^{20}D$ 1.5689.

Found %: C 45.90, 45.83; H 3.98, 4.03; [Cl + Br] 44.00, 43.92. $C_{10}H_{10}OClBr$. Calculated %: C 45.94; H 3.86; Cl 13.57; Br 30.51.

Methyllactolide of dimethyl-p-chlorobenzoylcarbinol (II, X = Cl) was prepared by the usual method. A transparent, mobile liquid with a pleasant odor. From 28 g of bromoketone and 20 g of sodium methoxide was obtained 17 g of methoxyoxide. Yield 74%.

• Experimental work by B. A. Gontarev.

B.p. 94-95° at 5 mm, $n^{20}D$ 1.5080.

Found %: C 62.43, 62.50; H 6.49, 6.44; Cl 16.81, 16.72; CH_3O 14.52, 14.40 $C_{11}H_{13}O_2Cl$. Calculated %: C 62.20; H 6.16; Cl 16.63; CH_3O 14.54.

Reaction with 2,4-dinitrophenylhydrazine in aqueous alcohol containing sulfuric acid gave the 2,4-dinitrophenylhydrazone of the ketoalcohol—dimethyl-p-chlorobenzoylcarbinol (see below).

Reaction of methyllactolide of dimethyl-p-chlorobenzoylcarbinol with benzoic acid was performed in benzene. Removal of the solvent left a colorless solid—the benzoic ester of dimethyl-p-chlorobenzoylcarbinol (IV, X = Cl). It was twice recrystallized from aqueous alcohol. M.p. 110-111°.

Found %: C 67.29, 67.17; H 5.09, 5.14; Cl 11.62, 11.51. $C_{17}H_{15}O_3Cl$. Calculated %: C 67.24; H 4.98; Cl 11.71.

Isomerization of methyllactolide of dimethyl-p-chlorobenzoylcarbinol to the methyl ester of methyl-p-chlorophenylacetylcarbinol (V, X = Cl) was effected by the method of [6] in presence of $ZnCl_2$. Yield of methyl ester 76%. A yellow liquid with a faint odor.

B.p. 118-119° at 9 mm, $n^{20}D$ 1.5245.

Found %: C 62.45, 62.21; H 6.35, 6.28; Cl 16.74, 16.88; OCH_3 14.61, 14.72. $C_{11}H_{13}O_2Cl$. Calculated %: C 62.20; H 6.16; Cl 16.63; OCH_3 14.54.

The 2,4-dinitrophenylhydrazone of the methoxyketone was recrystallized from a mixture of alcohol and ethyl acetate. Bright-yellow crystals, m.p. 93-94.

Found %: N 14.01, 14.09. $C_{17}H_{17}O_5N_4Cl$. Calculated %: N 14.22.

Dimethyl-p-chlorobenzoylcarbinol (III, X = Cl) was prepared by the action of sodium hydroxide on α-bromoisopropyl-p-chlorophenyl ketone in an aqueous alcoholic medium. Reaction of the bromoketone with alkali is violently exothermic, and the reactants must be well cooled before mixing. The medium must be kept alkaline throughout the whole process in order to preclude rapid conversion of the resulting alcohol to the anhydrodimer (VI). Yield 65-70%. The ketoalcohol was a fairly mobile liquid with a slight green tint and a pleasant odor; it was extremely unstable and easily changed into the anhydrodimer both when stored in the free state and in ethereal or alcoholic solution. It can be stored (in dilute solution) for about 24 hr. Anhydrodimerization is almost instantaneous in presence of acid.

B.p. 115-117° at 5 mm, $n^{20}D$ 1.5463.

Found %: C 60.60, 60.62; H 5.53, 5.61; Cl 17.71, 17.68. $C_{10}H_{11}O_2Cl$. Calculated %: C 60.42; H 5.55; Cl 17.84.

The ketoalcohol was characterized in the form of the 2,4-dinitrophenylhydrazone. Recrystallization from ethyl acetate gave beautiful golden scales with m.p. 180-181°. A mixture with the 2,4-dinitrophenylhydrazone prepared from the methyllactolide (see above) melted without depression.

Found %: N 14.65, 14.73. $C_{16}H_{15}O_5N_4Cl$. Calculated %: N 14.78.

Anhydrodimer of the ketoalcohol. Recrystallization from aqueous alcohol gave fine, lustrous crystals with m.p. 177-178°.

Found %: C 63.41; H 5.18. $C_{20}H_{20}O_3Cl_2$. Calculated %: C 63.50; H 5.30.

SUMMARY

1. Two methyllactolides of tertiary fatty-aromatic α-ketoalcohols containing substituents of different electrochemical characters in the benzene ring were prepared and characterized—the methyllactolides of dimethyl-p-anisoylcarbinol and of dimethyl-p-chlorobenzoylcarbinol.

2. It was shown that introduction of chlorine into the para position of the benzene ring leads to an increase (compared with the non-ring-substituted compound) of the rate of bromination of the ketone, of the rate of replacement of bromine by hydroxyl, and of the rate of transition of ketoalcohol to anhydrodimer.

3. Introduction of a methoxyl group into the para position of the benzene ring increases the hygroscopy of the corresponding methyllactolide and its tendency to hydrolyze.

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SYNTHESIS OF PRECURSORS AND FRAGMENTS OF ANTIBIOTICS

III. CONDENSATION OF TRICHLOROBUTADIENE WITH METHYL α-CHLOROACRYLATE

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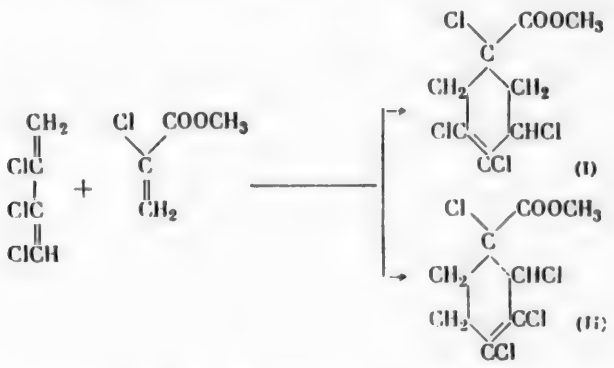
Original article submitted June 23, 1959

According to the literature [1], quinic acid is a precursor of antibiotics of the tetracycline series. With the aim of synthesizing quinic acid we investigated the dienic condensation of trichlorobutadiene with methyl α-chloroacrylate. The most extensively studied dienic condensations based on reaction of halobutadienes have been those involving chloroprene and bromophene [2] on the one hand and various dienophiles on the other. Concerning trihalobutadienes, the literature contains only general references to the possibility of utilization of 1,2,3-trichlorobutadiene [3] in dienic condensations. Actual dienic syntheses with use of this diene are not reported in the literature.

Our present investigation concerns the preparation of the previously undescribed methyl ester of 1,3,4,5-tetrachloro-Δ^3-cyclohexenecarboxylic acid. With this objective we carried out experiments on condensation of 1,2,3-trichlorobutadiene with methyl α-chloroacrylate. Reaction was effected under mild conditions (60°) and it can be represented as proceeding in two directions with formation of isomeric esters (I) and (II).



In our experiments we isolated one ester which appeared to correspond to formula (I). Special experiments were carried out to elucidate its structure. It was first subjected to relatively drastic thermal treatment (7 hr at 180° in an autoclave). A crystalline substance was thus obtained whose analysis and constants enabled it to be identified as 3,4-dichlorobenzoic acid, described in the literature [4]. The same acid was obtained when the reaction between the original diene and dienophile was carried out under the same drastic conditions. Formation of the compound could result from dehydrochlorination of (I) with loss of the labile chlorine atom at the carbon atoms in the 1 and 5 positions. A compound with structure (II) could not split off two molecules of hydrogen halide and lead to formation of 3,4-dichlorobenzoic acid. It should also be noted that structure (I) is supported by

the molecular refraction data. The structure of the ester implies the existence of stereoisomers. On prolonged standing the ester actually deposited a crystalline substance with m.p. 31.5°.

Judging by elementary analyses, the two substances (liquid and crystalline) are isomers. Their absorption spectra were different. They also behave differently when heated under drastic conditions: The crystalline product formed 3,4-dichlorobenzoic acid, and the liquid compound a substance with b.p. 120° (5 mm) and the formula $C_8H_7O_2Cl_3$. On the basis of the structure of the adduct represented by formula (I) we can assume formation of the methyl ester of 3,4,5-trichlorodihydrobenzoic acid. Our investigations thus show that adduct (I) exists in two stereoisomeric forms.

EXPERIMENTAL•

1,2,3-Trichlorobutadiene-1,3 (b.p. 56-65° at 26 mm, $n^{20}D$ 1.5262) was synthesized from vinylacetylene by the method of [5]. Methyl α-chloroacrylate (b.p. 41-44° at 28 mm, $n^{20}D$ 1.4420) was prepared from methyl acrylate [6].

Condensation of 1,2,3-trichlorobutadiene-1,3 with methyl α-chloroacrylate was effected in sealed glass ampoules in presence of hydroquinone or triethanolamine as stabilizer. Results of a series of experiments are presented in the table.

Condensation of Trichlorobutadiene with Methyl α-Chloroacrylate

Expt. No.	Amount of diene		Amount of dienophile		Yield (g)
	grams	moles	grams	mole	
1	20.5	0.13	15.7	0.13	8.8
2	23.6	0.15	18.15	0.15	9.7
3	23.6	0.15	12.0	0.10	7.3
4	5.1	0.032	31.1	0.25	3.0
5	32.6	0.20	4.0	0.033	6.5

Experiment 1. An ampoule was charged with 0.1 g of hydroquinone, 15.7 g of freshly distilled methyl α-chloroacrylate and 20.5 g of freshly distilled trichlorobutadiene (equimolar ratio of reactants). The ampoule was purged with nitrogen before sealing and then heated in a thermostat at 60°. After 48 hr a dark-yellow oil had formed, and from this the unreacted diene and dienophile were distilled off as an azeotropic mixture. Further distillation of the condensation product gave a fraction with b.p. 119-125° at 4 mm (8.8 g). This was found to contain a small quantity of hydroquinone crystals. The condensation product was freed of hydroquinone by treatment with 5% sodium bicarbonate solution, extraction with ligroine, drying with sodium sulfate and redistillation. A colorless oil boiling mainly at 124° (4 mm) was obtained. It partly crystallized on prolonged standing in the cold. Colorless druses with m.p. 31.5°, sparingly soluble in water, easily soluble in organic solvents. The ultraviolet absorption spectrum is plotted in the diagram (curve 1).

Found %: C 34.60, 34.61; H 2.88, 3.07; Cl 50.94, 51.35. $C_8H_8O_2Cl_4$. Calculated %: C 34.53; H 2.87; Cl 51.07.

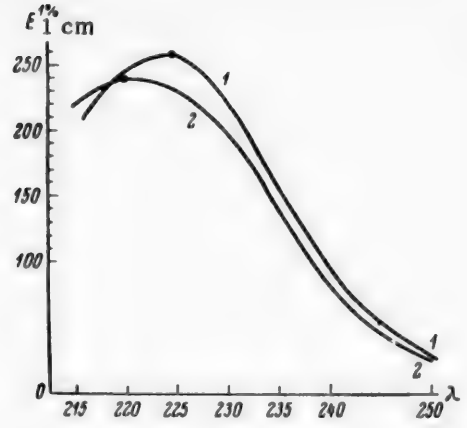
The oil remaining after separation of the crystals is soluble in the same solvents.

$n^{20}D$ 1.5321, d^{20}_4 1.4881, MR_D 57.88; calculated 57.03.

Found %: C 34.70, 34.88; H 3.05, 3.09; Cl 50.65, 50.66. $C_8H_8O_2Cl_4$. Calculated %: C 34.53; H 2.87; Cl 51.07.

The ultraviolet absorption spectrum in n-butanol is plotted in the diagram (curve 2).

•V. V. Konstantinova participated in the work.



Experiment 5 was carried out with a 6-fold excess of the diene and gave a higher yield of adduct—70.4% (calculated on the dienophile).

Preparation of 3,4-dichlorobenzoic acid. a) From trichlorobutadiene and methyl α-chloroacrylate. A 200-ml autoclave was charged with 0.1 g of hydroquinone, 23.3 g of trichlorobutadiene and 17.8 g of methyl α-chloroacrylate (equimolar ratio). Heating was carried out for 7 hr on an oil bath at 175-180°. The reaction mass was treated with steam. White crystals came down in the distillate and were extracted with ether. Removal of the ether from the extract left 9.2 g of solid, which after two recrystallizations from chloroform had m.p. 202.5°

Found %: C 44.15, 44.42; H 2.38, 2.30; Cl 36.66, 36.42. $C_7H_4O_2Cl_2$. Calculated %: C 43.97; H 2.09; Cl 37.17.

According to the literature 3,4-dichlorobenzoic acid melts at 201-203°; no depression in admixture with an authentic specimen. Yield 32.6% (on the dienophile).

b) From the crystalline isomer of the adduct. The crystalline isomer of the methyl ester of 1,3,4,5-tetrachloro-Δ^3-cyclohexenecarboxylic acid (1.3 g) with m.p. 31.5° was heated in an autoclave for 7 hr at 175-180°. A 56% yield of crystals with m.p. 202.5° was obtained. No depression in admixture with 3,4-dichlorobenzoic acid.

Preparation of substance with formula $C_8H_7O_2Cl_3$ from the liquid isomer of the adduct. The oil (2.0 g) with b.p. 124° at 4 mm was treated like the crystalline isomer. The resulting liquid product had b.p. 120° at 5 mm. Yield 0.9 g (52%).

Found %: C 39.43, 39.79; H 3.14, 3.20; Cl 43.23, 43.82. $C_8H_7O_2Cl_3$. Calculated %: C 39.75; H 2.89; Cl 44.09.

SUMMARY

1. The diene condensation of trichlorobutadiene with methyl α-chloroacrylate was studied.

2. It was shown that the reaction product is the methyl ester of 1,3,4,5-tetrachloro-Δ^3-cyclohexenecarboxylic acid, not previously described.

3. Two stereoisomeric esters were isolated: a liquid with b.p. 120° at 5 mm and a crystalline isomer with m.p. 31.5°.

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THE INTERACTION OF PHOSPHINE WITH ACETYLENIC α-OXIDES

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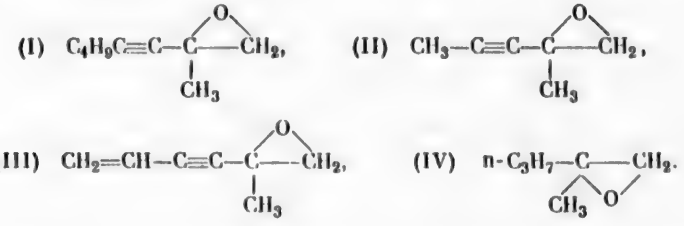
We previously demonstrated the possibility of conversion of products of condensation of α-acetylenic oxides with various nucleophilic reagents into heterocyclic systems containing atoms of O, S, Sr or N in a ring. In continuation of this work we studied the interaction of phosphine with α-acetylenic oxides with the objective of obtaining acetylenic hydroxyphosphines, of establishing the sequence of opening of the oxide ring, and of evaluating the influence of structural features of oxides on their reactivity. Both theoretical and practical interest is attached to the synthesis and study of the chemical properties of acetylenic hydroxyphosphines, because this class of compounds has not previously been described in the literature. Their potential practical interest is bound up with the possibility of their utilization as biologically active compounds. Conversion of these compounds into phosphorus-containing heterocycles also seemed possible. Methods of preparation of such compounds were not previously available. A convenient method of preparation of 1-phosphocyclopentadienes would open up broad perspectives in the field of the chemistry of phosphorophenes. We selected the following compounds as the starting point of our investigations:



Reaction of the oxides with sodium dihydrophosphide was effected in liquid ammonia at -60 to -40° [1]. Phosphine was obtained from phosphonium iodide by the method of [2]. Oxides (I) and (II) gave compounds (V) and (VI), whose constants are set forth in Table 1.

Oxide (III) rapidly reacts with sodium dihydrophosphide but the resulting product polymerizes completely. Reaction of oxide (IV) with sodium dihydrophosphide for 50 hr gave only traces of 2-methyl-2-hydroxypentylphosphine.

Attempts to synthesize benzyl-2-methyl-2-hydroxy-3-yne-octynylphosphine from oxide (I), sodium dihydrophosphide, and benzyl chloride in liquid ammonia in a single step were unsuccessful. The starting oxide (I) and tribenzylphosphine oxide were found in the products; the latter might be formed by the following sequence of reactions:

$$NaPH_2 + C_6H_5CH_2Cl \rightarrow C_6H_5CH_2PH_2 + NaCl$$
$$NaPH_2 + C_6H_5CH_2PH_2 \rightarrow C_6H_5CH_2PHNa + PH_3$$
$$C_6H_5CH_2PHNa + C_6H_5CH_2Cl \rightarrow (C_6H_5CH_2)_2PH + NaCl$$
$$(C_6H_5CH_2)_2PH + NaPH_2 \rightarrow (C_6H_5CH_2)_2PNa + PH_3$$
$$(C_6H_5CH_2)_2PNa + C_6H_5CH_2Cl \rightarrow (C_6H_5CH_2)_3P + NaCl$$
$$2(C_6H_5CH_2)_3P + O_2 \rightarrow 2(C_6H_5CH_2)_3PO$$

TABLE 1

Compound No.	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated
(V)	$C_4H_9C\equiv C-\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}-CH_2-PH_2$	64—65° (0.5)	1.4948	0.9360	53.30	52.99
(VI)	$CH_3-C\equiv C-\underset{\underset{CH_3}{|}}{\overset{\overset{OH}{|}}{C}}-CH_2-PH_2$	50—51 (1)	1.5063	0.9880	32.21	39.10

TABLE 2

Compound	P—H frequency (cm^{-1})
$Na_3HP_2O_5$ [6]	2271
$(C_2H_5)_2PH$ [7]	2270
P_2H_4 [8]	2286

The structure of phosphines (V) and (VI) was confirmed with the help of the infrared absorption spectra, which were obtained with the IKS-11 spectrograph in the 900-1800 cm^{-1} region using a NaCl prism and in the 1800-3800 cm^{-1} region using a LiF prism. Bands at about 1023 and 1070 cm^{-1} were probably caused by skeletal vibrations since they are encountered in 2-methyl-1,2-epoxypentyne-3, 1-diethylamino-2-methyl-2-hydroxypentyne-3 and 1-diethylamino-2-methyl-2-hydroxypentane.

According to the literature [3] the region of P-H bond vibrations is too narrow since it was investigated only in esters of phosphorus acids. In the two infrared absorption spectra of phosphines so far plotted, the P-H bond absorption does not occur in the region indicated above. It is known, for example, that the P-H vibrations in dimethylphosphine correspond to a frequency of 2290 cm^{-1} [4]. Phosphine itself absorbs at 2327 and 2421 cm^{-1} [5]; the Raman spectra of phosphorus compounds also exhibits a broader region of absorption of the P-H bond (Table 2).

Consequently in trivalent phosphorus compounds, the region in which the P-H bond can absorb extends from 2440 to 2270 cm^{-1}.

The experimental data show that the reactivity of oxides depends on their structure. Oxide (III) is more reactive than (I) and (II) because the conjugation between the oxide ring and the triple bond is intensified in (III).

The reaction of α-oxides with nucleophilic compounds under the conditions of alkaline catalysis starts with addition of an anion, and therefore an increased reaction rate is favored by use of a strongly basic solvent with a large dielectric constant.

Heating of hydroxyphosphines (V) and (VI) to 130-150° in presence of organic bases led to isolation of the compounds listed in Table 3.

TABLE 3

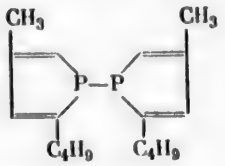
Dehydration products	Boiling point (pressure in mm)	$n^{20}D$	d^{20}_4	MR_D
Hydroxyphosphine (V)	188—140° (1)	1.5448	1.0010	96.73
Hydroxyphosphine (VI)	78 (0.5)	1.5832	1.0724	69.26

Combustion of the products of dehydration of hydroxyphosphines (V) and (VI) did not give consistent values for C and H or for P.*

Satisfactory C and H values were only obtained by combustion in a tube containing a platinum spiral and packed with pumice.

The individuality of the substances was confirmed in repeated syntheses and by the constancy of their physical constants after numerous fractional distillations. Structures were verified by the infrared absorption spectra of the product of dehydration of hydroxyphosphine (V) (IKS-11 spectrograph with NaCl and LiF prisms) and of the product of dehydration of hydroxyphosphine (VI) (LiF prism). Bands were found at about 793 and 836 cm^{-1}, which are caused by the deformation vibrations of the hydrogen at the double bond (790-840 cm^{-1} [3]); other bands are located at about 1606 cm^{-1}—associated with the conjugated double bond vibrations (close to 1600 according to [3])—and at 1162 and 1410 cm^{-1}, corresponding to the vibrations of the five-membered ring (close to 1150 and 1418). A band corresponding to the P-H bond vibrations was not detected.

On the basis of the empirical composition, molecular weight, method of preparation, spectral data and chemical properties, it appears that the following structure can be assigned to the compound prepared.



Investigations with the aim of conclusively establishing the structure of the products of dehydration of hydroxyphosphines are in progress.

EXPERIMENTAL

2,5-Dimethyl-5-hydroxy-1,2-epoxyoctyne-3. To the Grignard reagent prepared from 16.5 g of magnesium and 51 ml of ethyl bromide was slowly added 38.5 g of methylpropylethynylcarbinol. The mixture was then heated for an hour on a water bath. Dropwise addition was made to this mixture of 32 g of chloroacetone and the reaction mixture was left overnight. The mass was worked up in the usual manner to give 30 g (50%) of product.

B. p. 89° (0.5 mm), $n^{20}D$ 1.4618, d^{20}_4 0.9556, MR_D 48.38; calculated 48.02.

Found %: C 71.25; H 9.71. $C_{10}H_{16}O_2$. Calculated %: C 71.38; H 9.59.

The chlorohydrin corresponding to this oxide was not isolated since it readily polymerizes on distillation.

2-Methyl-1,2-epoxyoctyne-3 (I). a) To the Grignard reagent prepared from 9 g of magnesium and 40 g of ethyl bromide was added 30 g of hexyne-1. The mixture was then heated for an hour on a water bath. After dropwise addition of 35 g of chloroacetone (without cooling), the mixture was heated for about an hour on a water bath. After 8 hr, the organomagnesium complex was worked up in the usual manner to give 45 g (72%) of 1-chloro-2-methyloctyn-3-ol-2 with the following constants:

B. p. 58° (1 mm), $n^{20}D$ 1.4676, d^{20}_4 1.0019, MR_D 48.52; calculated 48.30.

b) To a solution of 40 g of the above-described chlorohydrin in 40 ml of absolute ether was added 26 g of KOH. The mixture was then heated for 6-10 hr on a water bath. The mass was worked up in the usual manner to give 18.8 g (60%) of (I). A colorless liquid giving a negative Beilstein test for halogen.

B.p. 48° (2-3 mm), d^{20}_4 0.8777, $n^{20}D$ 1.4474, MR_D 42.13; calculated 41.19.

Found %: C 78.12; H 10.30. $C_9H_{14}O$. Calculated %: C 77.65; H 10.13.

* This is apparently because (V) and (VI) break down on hydrolysis with liberation of phosphine, which goes off from the beaker for phosphorus determination, while the products of its oxidation are retained in the packed tube. It is known, moreover, that diphosphine breaks down at room temperature on exposure to diffused light and that breakdown is catalyzed by traces of oxygen and acids [8].

2-Methyl-2-hydroxy-3-yne-pentynylphosphine (VI). To a solution of sodium dihydrophosphide (prepared from 10 g of sodium) in liquid ammonia was added 31 g of 2-methyl-1,2-epoxypentyne-3. The mixture was stirred at -60 to -40° for 46 hr. The slurry remaining after evaporation of the ammonia was decomposed with water. Fractional distillation of the organic layer yielded 30.4 g (73%) of (VI).

Found %: C 55.74; H 8.64; P 23.61. $C_6H_{11}OP$. Calculated %: C 55.37; H 8.52; P 23.81.

2-Methyl-2-hydroxy-3-yne-octynylphosphine (V). The reaction mixture prepared from a solution of sodium dihydrophosphide (10 g of sodium) in liquid ammonia and 46 g of 2-methyl-1,2-epoxyoctyne-3 (I) was stirred for 80 hr. After the usual working-up, there was obtained 45.5 g (73%) of (V).

Found %: C 62.9; H 10.0; P 17.77. $C_9H_{17}OP$. Calculated %: C 62.76; H 9.95; P 17.99.

The hydroxyphosphines are colorless, readily mobile liquids with a characteristic phosphine odor, highly soluble in alcohol, ethyl acetate and ether, insoluble in water. They do not form derivatives with 2,4-dinitrochlorobenzene, p-toluenesulfochloride, phenyl isocyanate and picric acid. They are not hydrogenated over platinum black or Raney nickel.

Dehydration of 2-methyl-2-hydroxy-3-yne-octynylphosphine (V) by heating for half an hour 13 g of the substance with a few drops of diethylethylenediamine at 135-140° led to the product whose constants are given in Table 3.

The elemental analysis and the infrared absorption spectrum indicate the presence of a small quantity of the original hydroxyphosphine.

Preparation of mercury derivative of the product of dehydration of hydroxyphosphine (V). A few drops of the substance were dissolved in benzene and 1 ml of saturated aqueous solution of mercuric chloride was added. The precipitate was washed with water and dissolved in 96% alcohol. The alcohol was evaporated at room temperature. The white substance was dried over calcium chloride in vacuo. During the melting point determination the substance started to turn black at about 124° and melted at 128° with decomposition.

Oxidation with hydrogen peroxide. To a solution of 0.2 g of the compound in alcohol was added several milliliters of 30% hydrogen peroxide. The solvent was then evaporated. This operation was repeated. The resulting white substance was crushed to a powder and dried over phosphorus pentoxide in vacuo. It dissolves readily in water and alcohol, and is insoluble in benzene, ligroine and ether. M.p. 80-90°.

Found %: C 47.12; H 7.60; P 12.67. $C_{18}H_{36}O_9P_2$. Calculated %: C 47.16; H 7.90; P 13.21.

Oxidation with potassium permanganate. Oxidation of 4.61 g of the compound was effected, with cooling, by 17.4 g of potassium permanganate over a period of 2.5 days. From the neutral, steam-distillable products was obtained a 2,4-dinitrophenylhydrazone [9] which after recrystallization from alcohol melted at 105-107°. No depression in admixture with the 2,4-dinitrophenylhydrazone of methyl n-butyl ketone (m.p. 106°). The quantity of product was too small to permit an elemental analysis. The silver salts obtained from the volatile acids decomposed quickly even in red light. The residue in the flask after distillation of the volatile acids consisted of brown, oily drops which after drying in vacuo over phosphorus pentoxide could be triturated to form a yellow hygroscopic powder. The latter could not be recrystallized from common organic solvents. M.p. 98-102° (from ethyl acetate).

Found %: C 50.62; H 8.20; P 14.88. M 790, 820. $C_{18}H_{36}O_7P_2$. Calculated %: C 50.82; H 8.29; P 14.57. M 425.34.

The nonvolatile acids were brought down by an aqueous solution of 2,4-dinitrophenylhydrazine hydrochloride. The resulting hydrazone resinified when recrystallization was attempted from alcohol and acetic acid. The noncrystalline hydrazone melted at 122-124°; combustion gave (%): C 49.5; H 7.0. Phosphorus was determined only qualitatively because the quantity of substance was too small to permit quantitative analysis.

SUMMARY

1. The reaction of sodium dihydrophosphide with the following oxides was studied: 2-methyl-1,2-epoxypentyne-3; 2-methyl-1,2-epoxyoctyne-3; 2-methyl-1,2-epoxyhexen-5-yne-3; and 2-methyl-1,2-epoxypentane.

2. The first representatives of the hydrophosphines of the acetylenic series were isolated: 2-methyl-2-hydroxy-3-yne-pentynylphosphine and 2-methyl-2-hydroxy-3-yne-octynylphosphine.

3. Infrared spectra of the hydroxyphosphines were plotted and the characteristic frequency of the P-H bond was found (2270-2440 cm^{-1}).

4. The product of dehydration of the first hydroxyphosphine was prepared and characterized. It probably has the structure of dibutyl-(2,2')-dimethyl-(4,4')-P-diphospha-(1,1')-dicyclopentadiene, i.e. (2,3-4,5)-bis-butyl-(2)-methyl-(4)-phosphorophene.

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HOMOLOGS OF MONOVINYLACETYLENE

IX. CHARACTERISTICS OF ENYNIC HYDROCARBONS CONTAINING TERT-BUTYL AND ISOPROPYL GROUPS

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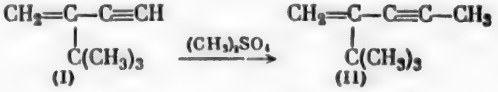
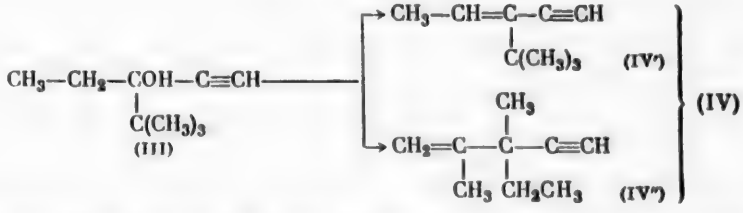
We previously [1] drew attention to the anomalous optical characteristics of the hydrocarbon 3',3'-metho-3-ethylbuten-3-yne-1 (I). We suggested that the absence of exaltation of molar refraction and the two low relative dispersion of the hydrocarbon might be associated with noncoplanarity of the system due to steric hindrance by the tert-butyl group. The present work is devoted to the synthesis and study of the optical properties of some sterically screened enynic hydrocarbons containing tert-butyl and isopropyl groups.

Methylation of hydrocarbon (I) in liquid ammonia gave hydrocarbon (II) (4',4'-metho-4-ethylpenten-4-yne-2). Its structure was confirmed by hydrogenation to a saturated hydrocarbon whose constants are the same as those of 2,2,3-trimethylhexane.

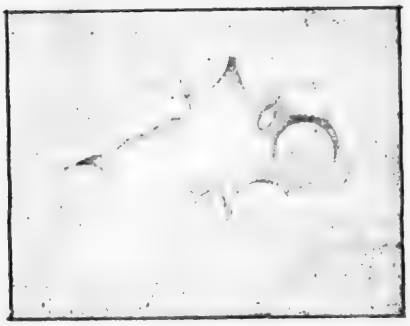


We constructed a Stewart model of the molecule of (II) which shows that the tert-butyl group does not prevent the double and triple bonds from existing in the same plane (see figure).

Dehydration of the alcohol 4,4-dimethyl-3-ethylpentyn-1-ol-3 (III) is especially interesting in connection with a study of the dehydration of tertiary acetylenic alcohols containing the neopentyl grouping.



In the preceding paper [1] an attempt was made to obtain spectral proof of the structure of the products of dehydration of methyl-tert-butylethynylcarbinol with the aim of detecting possible rearrangement with alteration of the carbon framework. Unequivocal evidence for the course of dehydration was obtained from the infrared spectrum, the valence vibrations of the double and triple bonds corresponding to conjugated bond vibrations. In the present case the isomeric hydrocarbons (IV') (3',3'-metho-3-ethylpenten-3-yne-1) and (IV") (3,4-dimethyl-3-ethylpenten-4-yne-1) are characterized by different atomic groupings: Hydrocarbon (IV')—the product of normal dehydration—must contain a trisubstituted double bond, whereas the product of rearrangement (IV") will contain a terminal methylene group. The presence of these different groups greatly facilitates



Model of the 4',4'-metho-4-ethylpenten-4-yne-2 molecule.

analysis of the products of dehydration both by spectral and chemical methods. The strong absorption bands at 903 and 3087 cm^{-1} in the spectrum of (IV) indicate the presence of a mixture of substances. The above-mentioned rearrangement or isomerization of the hydrocarbon with a double-bond shift may account for the development of these bands, which are characteristic of absorption of a terminal methylene group. Similar cases of isomerization of enynic hydrocarbons have been described in the literature [2]. In the same way we might account for the absorption frequencies of the valence vibrations of the trisubstituted olefinic bond (1648 cm^{-1}) and the monosubstituted acetylenic bond (2100 cm^{-1}), both of which are abnormally high for a conjugated bond system. It is evident that spectrographic data alone cannot serve as a basis for solution of the problem of the structure and ratio of the isomeric hydrocarbons. An impending publication will give the chemical evidence for the structure of the mixture of hydrocarbons on the basis of quantitative determination of all the products of ozonolysis.

Dehydration of 5-methyl-4'-metho-4-ethylhexyn-2-ol-4 (V) over unfired porcelain gave hydrocarbon (VI)—5-methyl-4'-metho-4-ethylhexen-4-yne-2— in 66% yield; the infrared spectrum of the latter contains bands in the absorption regions of multiple bonds, indicating the presence of a system of conjugated bonds. However, this conclusion must be confirmed by data for the Raman spectrum since the absorption of fully substituted double and triple bonds is more clearly reflected in the Raman spectrum.

$$(CH_3)_2CH-\underset{\displaystyle CH(CH_3)_2}{\overset{\displaystyle |}{C}}(OH)-C\equiv C-CH_3 \rightarrow (CH_3)_2C=\underset{\displaystyle CH(CH_3)_2}{\overset{\displaystyle |}{C}}-C\equiv C-CH_3$$

(V) (VI)

It is interesting to compare the results of dehydration of carbinol (V) with our data for dehydration of diisopropylethynylcarbinol [3]. Under the same conditions the latter formed a monomeric hydrocarbon in very poor yield (of the order of 3-5%).

In our earlier publications [4] and in A. I. Zakharova's paper [5] a marked difference was noted between the reactions of substituted acetylenic alcohols containing the neopentyl grouping—methyl-tert-butylethynylcarbinol—and those of methy-tert-butylmethylethynylcarbinol. These examples demonstrated particularly clearly the exceptional influence of the presence of a methyl group in place of a free acetylenic hydrogen on the mechanism of substitution. Whereas in the case of monosubstituted α-acetylenic alcohols an acetylenic residue lowers the electron density at the central carbon atom and thereby promotes a bimolecular course of the substitution reaction, the replacement of the free acetylenic hydrogen by a methyl group has the opposite effect due to a change in the electron density distribution in the molecule. A. I. Zakharova [5] reports that the positive inductive effect of the methyl group, reinforced by the conjugation effect, increases the electron density at the central carbon atom, and this in turn increases the mobility of the hydroxyl and favors a monomolecular course of the substitution reaction. This interpretation has been supported in recent years by kinetic investigations of the hydrolysis of acetylenic chlorides [6]. In the light of these data we can understand why water splits off from carbinol (V) more easily than from its analog containing a terminal acetylenic group.

Results of determinations of the physical constants of the prepared hydrocarbons are presented in the table. The first three hydrocarbons (containing a tert -butyl group) are characterized by the absence of exaltation of molar refraction and by an anomalously low relative dispersion [7]. But since we had established that products of dehydration of carbinol (III) are a mixture of isomeric hydrocarbons, it would be premature to draw any final conclusions about the influence of the tert-butyl group on the optical properties of enynic hydrocarbons. An unconjugated hydrocarbon is possibly present as an impurity and may be the cause of the anomalous values.

Hydrocarbons	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	n_F^{20}	n_C^{20}	MR_D found	MR_D calculated	EM_D	ω_{FCD}
$CH_2=C(C(CH_3)_3)-C\equiv CH$ (I)	47° (130)	0.7609	1.43147	1.43934	1.42841	36.74	36.67	0.07	25.33
$CH_2=C(C(CH_3)_3)-C\equiv C-CH_3$* (II)	79—80 (130)	0.7887	1.45126	1.45956	1.44798	41.66	41.29	0.37	25.66
C_9H_{14} (IV)	72 (130)	0.7837	1.44296	1.45084	1.43986	41.33	41.29	0.04	24.79
$(CH_3)_2C=C(HC(CH_3)_2)-C\equiv C-CH_3$ (VI)	76 (45)	0.8034	1.46677	1.47607	1.46307	47.02	45.91	1.11	27.85

*Hydrocarbon (II) was also obtained by dehydration of 3,5,5-trimethylhexyn-2-ol-4; the constants were identical with the above.

EXPERIMENTAL

4',4'-Metho-4-ethylpenten-4-yne-2 (II). Into a test tube immersed in a Dewar vacuum flask were poured 250 ml of liquid ammonia and 50 g of 3',3'-metho-3-ethylbuten-3-yne-1. The mixture was stirred vigorously while 10.7 g of metallic sodium was added in the course of 4 hr; this operation was followed by dropwise addition of 50.3 g of dimethyl sulfate. The reaction was performed at -38°. The resulting reaction mixture was stirred for another 2 hr and then stood overnight (during this period the test tube was removed from the Dewar flask and topped by a condenser). The next day water was carefully run into the test tube until the precipitate had completely dissolved. The hydrocarbon was extracted with ether, dried over potassium carbonate and distilled in a column in a nitrogen atmosphere. Yield 38%. The constants of the hydrocarbon are given in the table.

Found %: C 88.62; H 11.67. C_9H_{14}. Calculated %: C 88.45; H 11.55.

The following absorption bands were found in the spectrum (IKS-11 apparatus, NaCl and LiF prisms) (cm^{-1}): 896 s; 960 w; 1050 m; 1123 w; 1201 m; 1247 s; 1365 s; 1387 m; 1398 m; 1442 s; 1624 m; 1701 w; 2090 w; 2210 m; 2244 m; 2861 m; 2952 w; 3096 s. [Note: s = strong; w = weak; m = medium.]

Hydrogenation of the hydrocarbon (4.68 g of substance in 25 ml of alcohol) over platinum black (0.6 g of Pt) led to absorption of 2621 ml of H_2 (0°, 760 mm) (theoretical amount 2600 ml). The product (2,2,3-trimethylhexane) was separated and after distillation had the following constants in agreement with the literature [8].

B.p. 126-127° (752 mm), $n^{20}D$ 1.40925, $n^{20}F$ 1.41427, $n^{20}D$ 1.40712. ω_{FCD} 17.47, d^{20}_4 0.7325, MR_D 43.42.

4,4-Dimethyl-3-ethylpentyn-1-ol-3 (III) was prepared by the A. E. Favorskii reaction—condensation of 2,2,-dimethylpentanone-3 with acetylene in presence of potassium hydroxide powder. Yield 50%.

B.p. 94° (90 mm), d^{20}_4 0.8720, $n^{20}D$ 1.4456, MR_D 42.95; calculated 43.28.

Found %: C 76.92; H 11.46. $C_9H_{16}O$. Calculated %: C 77.08; H 11.41.

Dehydration of 4,4-dimethyl-3-ethylpentyn-1-ol-3 was carried out over unfired porcelain in a nitrogen stream at 300°. The resulting hydrocarbon gave a positive test for free acetylenic hydrogen with ammoniacal silver oxide and rapidly changed in the air. Its constants are given in the table.

Found %: C 88.57; H 11.84. C_9H_{14}. Calculated %: C 88.45; H 11.55.

Hydrogenation of the hydrocarbon was carried out in presence of platinum black: 1.33 g of hydrocarbon in 25 ml of alcohol, 0.14 g Pt; 908 ml of H_2 (0°, 760 mm) absorbed (theoretical requirement 896 ml).

The spectrum of the hydrocarbon was taken in the 3-12 mμ region with the IKS-11 spectrograph (NaCl and LiF prisms). Found (in cm^{-1}): 820 m; 860 s; 903 s; 924 w; 933 w; 970 w; 1024 m; 1053 m; 1145 w; 1201 m; 1259 s; 1370 m; 1378 m; 1462 m; 1648 m; 1704 s; 2100 m; 2873 w; 2914 w; 2937 m; 3048 w; 3087 m; 3305 s.

5-Methyl-4'-metho-4-ethylhexyn-2-ol-4 (V). A solution of 81 g of ethyl bromide in twice the quantity of ether was added dropwise to 18 g of magnesium turnings. The resulting ethylmagnesium bromide was diluted with a large volume of ether. Methylacetylene was passed into the reaction medium, which was ice cooled and vigorously stirred. After the reaction mixture had separated into layers, diisopropyl ketone (45 g) was added to the flask. After 48 hr the organomagnesium complex was cautiously decomposed first with water and then with 10% hydrochloric acid. The ethereal solution was neutralized with sodium carbonate, washed with water and dried with potassium carbonate. Yield 75%.

B.p. 99° (45 mm), $n^{20}D$ 1.4560, d^{20}_4 0.8818 MR_D 47.55; calculated 47.90.

Found %: C 77.98; H 11.73. M 155.1. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.76. M 154.24.

Hydrogenation of the carbinol was carried out over platinum black: 1 g of substance in 25 ml of alcohol, 0.1 g Pt; 310 ml H_2 taken up (0°, 760 mm), compared with the theoretical requirement of 292 ml.

Dehydration of 5-methyl-4'-metho-4-ethylhexyn-2-ol-4 was performed over unfired porcelain at 330° in a CO_2 stream; hydrocarbon (VI) was obtained in 66% yield; constants are given in the table.

Found %: C 88.12; H 11.87; 559 ml H_2 (0°, 760 mm) taken up. $C_{10}H_{16}$. Calculated %: C 88.15; H 11.85 theoretical H_2 requirement 544.7 ml (1.10 g substance, 0.07 g Pt).

The spectrum was taken with the IKS-11 instrument (NaCl and LiF prisms). Found (in cm^{-1}): 896 w; 924 w; 956 w; 1012 w; 1076 s; 1170 m; 1202 m; 1364 s; 1384 vs; 1456 s; 1650 w; 1718 w; 2099 w; 2212 w; 2873 s; 2904 m; 2962 s.

SUMMARY

1. Methylation of 3',3'-metho-3-ethylbuten-3-yne-1 in liquid ammonia gave 4',4'-metho-4-ethylpenten-4-yne-2.

2. Dehydration over unfired porcelain of the tertiary acetylenic alcohol 5-methyl-4'-metho-4-ethylhexyn-2-ol-4 gave 5-methyl-4'-metho-4-ethylhexen-4-yne-2.

3. Spectroscopic examination of the products of dehydration of 4,4-dimethyl-3-ethylpentyn-1-ol-2 led to identification of the product as a mixture of isomeric hydrocarbons C_9H_{14}.

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RADICAL AND IONIC REACTIONS OF TETRAETHYLTHIURAM DISULFIDE

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Considerable theoretical interest is attached to a study of the reactions of tetraethylthiuram disulfide. It is also of no small practical value since the thiuram participates in processes of vulcanization and degradation of rubbers [1, 2]. According to the vulcanization mechanism of Farmer and Bloomfield [1, 3], sulfur reacts with the hydrogen of the α-methylene group to form a polysulfide bond. The thiuram activates this process by a mechanism that is still obscure. It is known to be the active degrading agent for rubbers of the thiokol type, which are cleaved at the sulfide bond. Thiuram degradation is also encountered with other types of polymers whose molecules contains a very small number of polysulfide bonds, e.g. polychloroprene.

In order to gain an insight into these reactions, we must make a closer study of some properties of the thiuram.

Radical breakdown of the thiuram. The literature does not contain any experimental proofs of the radical breakdown of the thiuram, although Koch [5] mentions the possibility of such a breakdown on the basis of the observation that heated thiuram solution develops a color that disappears on cooling. Employment of the thiuram as an initiator of chloroprene polymerization in bulk [6] is indirect evidence of such a type of breakdown; but no products of its radical breakdown have previously been isolated.

We studied the radical breakdown of the thiuram in a carbon tetrachloride medium in the absence of an initiator at 145°. The compound $(C_2H_5)_2N-\overset{\overset{S}{\|}}{C}-SCl$ was isolated in a yield of 46%; it could only have been formed by reaction of the $(C_2H_5)_2N-\overset{\overset{S}{\|}}{C}-S\cdot$ radical with CCl_4. The products of the reaction also included carbon disulfide and a compound whose analysis corresponded to the formula $(C_2H_5)_2NCl$ and which contained a saponifiable chlorine atom. The two latter compounds are evidently the consequence of secondary reactions of thiuram radicals with CCl_4.

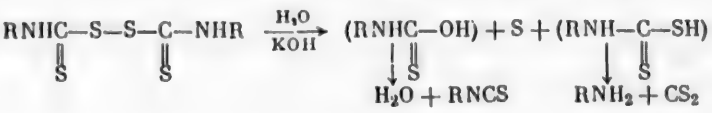
$$(C_2H_5)_2N-\overset{\overset{S}{\|}}{C}-S\cdot \rightarrow (C_2H_5)_2N\cdot + CS_2$$

$$(C_2H_5)_2N\cdot + CCl_4 \rightarrow (C_2H_5)_2NCl + CCl_3$$

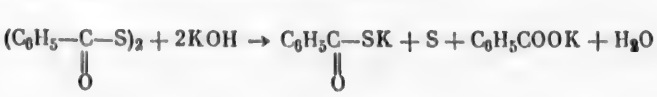
Radical decomposition of the thiuram thus gave the following products:

$$(C_2H_5)_2N-\overset{\overset{S}{\|}}{C}-SCl\ 46\%,\quad (C_2H_5)_2NCl\ 44\%,\quad CS_2\ 43\%.$$

Ionic reactions of the thiuram. Tetramethyl- and tetraethylthiuram disulfides react with potassium cyanide in aqueous alcoholic solution with loss of one sulfur atom and they form thiuram monosulfide [7]. In the opinion of some authors, this is the basis of the activity of thiuram disulfides as vulcanizing agents for rubber [8, 9]. Data for the breakdown of dialkylthiuram disulfides in presence of water and alkali are reported in the literature [10].

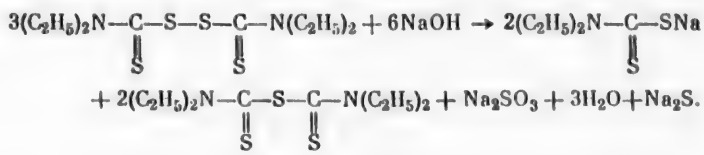


All sulfides with this type of structure react similarly [11].



No data have been published for reaction of tetrasubstituted thiuram disulfides with alkali. We showed that these reactions have a different mechanism than that for dialkyl derivatives which contain a mobile hydrogen atom at the nitrogen and are therefore more reactive and less heat-resistant than tetra-substituted derivatives.

We studied the reaction of tetraethylthiuram disulfide with NaOH and NH_4OH. The results indicated the possibility of the following mechanism.



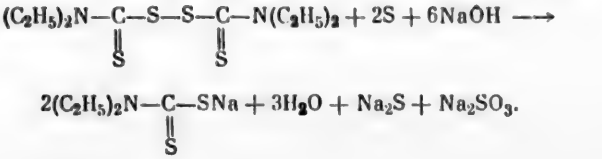
Ammonia behaves like caustic alkali except that reaction is slower due to the lower basicity (see table).

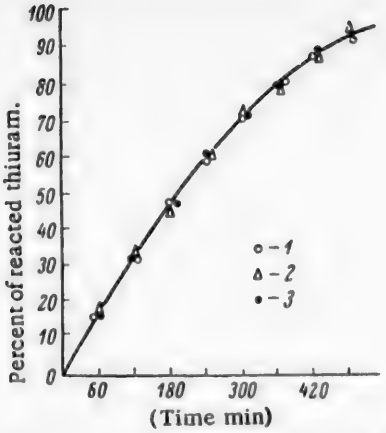
Reaction of Tetraethylthiuram Disulfide with Bases

Name of base	Concentration of base (%)	Reaction period (hr)	Reaction products (in % of original thiuram)			
			unreacted thiuram	thiuram monosulfide	diethyldithiocarbamate	sulfur split off (calculated on the tetraethylthiuram monosulfide)
NaOH (aqueous)	2.0	8	–	58.0	31.0	98.0
NaOH (alcoholic)	2.0	6	31.0	40.0	22.0	93.0
NH_4OH (aqueous)	2.0	8	45.0	32.0	15.2	92.0
NH_4OH (alcoholic)	2.0	6	65.0	17.0	10.0	89.0

According to the table the ratio of diethyldithiocarbamate to thiuram monosulfide in all cases is 1 : 2, in harmony with the reaction equation given above.

The thiuram was reacted with alkali in presence of elemental sulfur with the objective of obtaining confirmation of the proposed mechanism. Thiram monosulfide was not found among the reaction products, the tetraethylthiuram disulfide being converted nearly quantitatively (95.4%) into sodium diethyldithiocarbamate. In addition, Na_2S and Na_2SO_3 were formed in the quantities required by the equation:





Influence of an initiator ($K_2S_2O_8$) and an inhibitor (Neozone D) on the rate of reaction of thiuram with alkali. 1) Without initiator; 2) 3% $K_2S_2O_8$. 3) 2% Neozone D.

The absence of thiuram monosulfide from the reaction products confirms the assumption that its formation is associated with detachment of sulfur.

Confirmation of the ionic character of the reaction of thiuram with alkali was obtained by a study of the kinetics of this reaction in presence of an initiator (potassium persulfate) and an inhibitor (phenyl-β-naphthylamine—Neozone D). We see from the figure that neither of these additives influences the rate of reaction of thiuram with caustic alkali. This result justifies the assumption that reaction of thiuram with alkali is ionic in character.

Reaction of tetraethylthiuram disulfide with diethylamine. This reaction has been studied by several investigators [12-14]. Délépine [12] reported the formation of dimethylammonium-thiocarbamate, sulfur and tetramethylthiourea. According to Bedford and Gray [13] carbon disulfide is formed instead of thiourea. Graig and Davidson [14] carried out the reaction at 50° (previous investigators had worked at 100°) in presence of a 5-fold excess of diethylamine. They found that the reaction goes in accordance with the equation

$$(CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}S{-}S{-}\overset{\overset{S}{\|}}{C}{-}N(CH_3)_2 + 2HN(CH_3)_2 \longrightarrow$$

$$(CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}S{-}NH_2(CH_3)_2 + (CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}S{-}N(CH_3)_2$$

(A)

The second product breaks down during vacuum distillation and gives tetramethylthiuram disulfide, tetramethylthiourea and tetramethyldiaminosulfide.

$$3(CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}S{-}N(CH_3)_2 \longrightarrow (CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}N(CH_3)_2 +$$

$$(CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}S{-}S{-}\overset{\overset{S}{\|}}{C}{-}N(CH_3)_2 + (CH_3)_2N{-}S{-}N(CH_3)_2$$

We reacted tetraethylthiuram disulfide with diethylamine at 60° and isolated tetraethyldiaminodithiocarbamate (A) in accord with the mechanism of Graig and Davidson. Other products of the reaction were not examined.

EXPERIMENTAL

Radical breakdown of the thiuram. 3 g (0.01 mole) of tetraethylthiuram disulfide (t.e.t.d.) was heated in 30 g (0.2 mole) of carbon tetrachloride in a sealed ampoule in a nitrogen atmosphere for 8 hr at 145-150°. The following products were isolated:

1) Crystals soluble in benzene (1.68 g); m.p. 46-46.5°.

Found %: S 34.9; Cl (total) 19.47; Cl (saponifiable) 19.5; N 7.82. M 187.3. $C_5H_{10}NS_2Cl$. Calculated %: S 34.88; Cl (total) 19.3; Cl (saponifiable) 19.3; N 7.75. M 183.5.

2) Crystals insoluble in the majority of organic solvents (0.92 g). This substance deliquesced in the air and did not melt (blackened and charred when heated to 170-180°).

Found %: N 12.89; Cl 33.04. $(C_2H_5)_2NCl$. Calculated %: N 13.0; Cl 32.98.

3) Carbon disulfide (0.66 g); this was determined by the following procedure: After opening the ampoule, a weighed amount of CCl_4 was shaken with alcoholic caustic alkali, the excess alkali was neutralized, and the resulting xanthate titrated with iodine.

Reaction of tetraethylthiuram disulfide with alkali. A heated benzene solution of 5 g (0.017 mole) of t.e.t.d. was stirred for 8 hr with an aqueous (or alcoholic) solution of NaOH (70 g of 2% solution or 0.034 mole). The following were obtained:

1) Tetraethylthiuram monosulfide (2.6 g or 58% of the original thiuram). Crystals with m.p. 64-65°.

Found %: S 36.36; N 10.2. M 259.0. $C_{10}H_{20}N_2S_3$. Calculated %: S 36.36; N 10.38. M 264.0.

2) Sodium diethyldithiocarbamate (2.35 g). This was separated after evaporation of the aqueous layer. It represented 31% of the original thiuram. After recrystallization from aqueous alcohol it had m.p. 94-96°. The literature [5] gives m.p. 92-102° and mentions that the substance crystallizes with three molecules of water.

Found %: S 28.4; N 6.05; Na 10.0. $C_5H_{10}NS_2Na \cdot 3H_2O$. Calculated %: S 28.55; N 6.22; Na 10.22.

The Na_2S and Na_2SO_3 contents were determined by the following procedure: A sample of the aqueous layer was oxidized with iodine. The sodium diethyldithiocarbamate was converted to the thiram and came down. Sodium sulfide reacted with iodine to give NaI and elemental sulfur which came down with the thiram. The mixed precipitate of sulfur and thiuram was treated with 10% aqueous alkali solution in the cold. The sulfur dissolved in the alkali (thiuram does not react with alkali under these conditions). After oxidation of the sulfur solution in alkali with bromine water and nitric acid, the sulfur was determined as barium sulfate. Iodine converted the Na_2SO_3 to sulfate, which was determined as $BaSO_4$.

Material balance of an experiment. Amount of thiuram taken 5 g; amount of diethyldithiocarbamate obtained 2.35 g; amount of tetraethylthiuram monosulfide 2.60 g; sulfur in form of Na_2S 0.16 g; sulfur in form of Na_2SO_3 0.17 g.

Reaction of thiuram with alkali in presence of elemental sulfur. A solution in 100 g of benzene of 10 g (0.0338 mole) of t.e.t.d. was heated with 2.2 g (0.07 mole) of elemental sulfur and 165 g of 5% NaOH solution (0.2 mole). There was obtained 14.5 g (95.4%) of sodium diethyldithiocarbamate.

Found %: S 28.7; N 6.33. $C_5H_{10}NS_2Na \cdot 3H_2O$. Calculated %: S 28.55; N 6.22. Amount of sulfur in Na_2S form 0.98 g (44.8%). Amount of sulfur in Na_2SO_3 form 0.95 g (43.8%).

Reaction of t.e.t.d. with diethylamine. A solution of 2.46 g (0.034 mole) of diethylamine in 20 ml of water was heated with 5 g (0.017 mole) of t.e.t.d. at 60° for 8 hr. After the later had been separated and the aqueous layer evaporated, 3.2 g of crystals was isolated; m.p. 48-49°. Oxidation with iodine led to quantitative conversion to the thiram.

SUMMARY

1. The conditions for radical breakdown of tetraethylthiuram disulfide in carbon tetrachloride are studied and it is shown that at 145° the thiuram breaks down to radicals which react with CCl_4 to form the compounds $(C_2H_5)_2N-\underset{\underset{S}{\|}}{C}-SCl$, $(C_2H_5)_2NCl$, and CS_2.

2. The quantitative composition of the products of breakdown of tetraethylthiuram disulfide in presence of alkali is established. The kinetics of this reaction are studied and it is found that neither initiators ($K_2S_2O_8$) nor inhibitors (Neozone D) influence the rate of this reaction, so that an ionic mechanism is indicated.

3. It is shown that one of the products of reaction of tetraethylthiuram disulfide with diethylamine is tetraethyldiaminodithiocarbamate.

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POLYMETHYLENE RINGS

XXXIV. ABSORPTION SPECTRA OF HYDRAZONES OF DIBENZOSUBERANEDIONE-6,7 AND BENZIL

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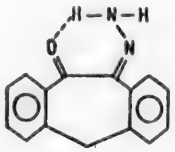
Original article submitted December 30, 1958

In the preceding investigation [1] we obtained dibenzosuberanedione-6,7 monohydrazone (I) and studied its chemical properties. We explained its behavior by its syn-configuration and by the presence of a chelate ring.



(I)

In the present work we undertook an investigation of the ultraviolet and infrared absorption spectra. For comparison purposes we plotted the spectra of the following compounds, which were prepared by the literature methods: dibenzosuberanedione-6,7 monoxime (II) [2], benzil monohydrazone (III) [3], the two isomeric benzil dihydrazones (m.p. 150° (IV) [4] and m.p. 197° (V) [5]) and benzoin hydrazone (VI) [6].

Ultraviolet Spectra

The position and intensities of the absorption maxima are set forth in Table 1 and the absorption curves are plotted in Figs. 1 and 2.

The spectra of the monohydrazones (I) and (III) each contain two strong maxima which reflect a similarity of structure. The spectra of the monohydrazones are simpler than those of the corresponding diketones. They are deficient in a long-wave maximum in the 400 mμ region which, according to Leonard [2, 7], characterizes the α-diketonic grouping. The absorption curve of dibenzosuberanedione-6,7 (II) has one maximum and an inflection at 350 mμ, i.e., at the frequency characteristic of absorption of the monohydrazone (I). The spectra of each of the isomeric monoximes of benzil (studied by Meisenheimer [8]) and those of benzil dihydrazone (IV) and benzoin hydrazone only contain one maximum.

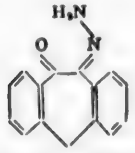
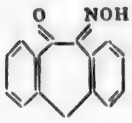
Infrared Spectra

The frequencies of the absorption bands of solutions in $CHCl_3$ are set forth in Table 2; figures in brackets are the frequencies of the solid hydrazones. Absorption curves are plotted in Fig. 3.

In the region of the valence vibrations of the OH and NH groups of the monohydrazones (I) and (III) and of the dihydrazone (IV) of benzil, three maxima are observed which correspond to the free amino group and to the amino group with a hydrogen bond. We were unable to establish whether or not these compounds contain

TABLE 1

Position of Absorption Maxima for Compounds (I), (II), (III), (IV), (VI)

Formula	Compound No.	λmμ	log κ	λmμ	log κ
	(I) *	245	4.08	348	3.84
$C_6H_5C(=O)-C(=NNH_2)C_6H_5$	(III)	253	4.05	295	4.05
$C_6H_5C(=NH_2N)-C(=NNH_2)C_6H_5$	(IV)	275	4.39		
$C_6H_5CH(OH)-C(=NNH_2)C_6H_5$	(VI)	250	3.40		
	(II)	275	4.08	~350	2.4

* The absorption curve of dibenzosuberanedione-6,7 (I) does not depend on the solvent, in harmony with our conclusion (based on the chemical properties of the substance [1]), that (I) is not tautomeric.

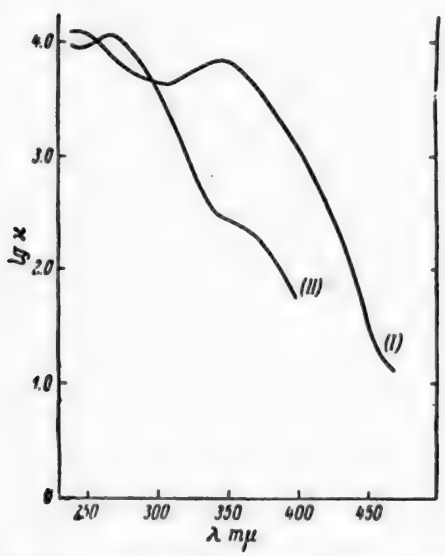


Fig. 1. Ultraviolet absorption curves of the monohydrazone (I) and monoxime (II) of dibenzosuberanedione-6,7.

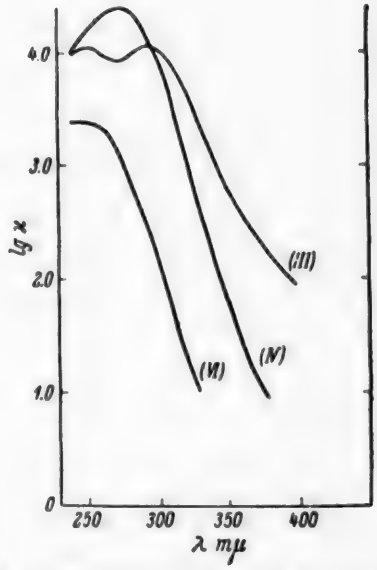
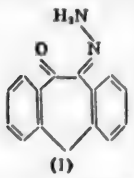
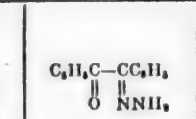
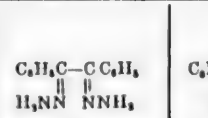
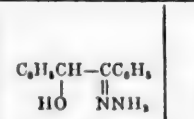
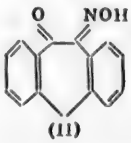


Fig. 2. Ultraviolet absorption curves of the monohydrazone (III) and dihydrazone (IV) of benzil and the hydrazone (VI) of benzoin.

TABLE 2

Frequencies of Absorption Bands of Compounds (I), (II), (III), (IV), (VI) in Chloroform Solution (in cm^{-1})

	 (I)	 (III)	 (IV)	 (VI)	 (II)
NH	3340 s 3340 w	3398 s 3295 s	3344 s 3268 w		
OH	3140 m	3196 s	3190 m		3200 broad
C=O	1620 s (1607)	1647 s (1627)			1665 s (1674)
Ph Ph–C=	1604 s	1607 s	1620 s 1587 s	1610 s ~1580	1604 s ~1573
C=N	1543 s ~1522	1565 s	1565 s 1522 w	1560 s	~1544 1529 m
Ph	1484	1492 s	1492	1492 s	1502 s

intramolecular hydrogen bonds, since the hydrazones are sparingly soluble in CCl_4 and we could not examine their solutions, but the bands at 3140-3190 cm^{-1} indicate the possibility of such a bond.

In the case of compound (II) we observed one broad and weak band which had previously been detected by Leonard [2]. A clear spectrum could not be obtained for benzoin hydrazone in this region.

A similar picture has been observed [9] for the monophenylhydrazones of the naphthoquinones. For 1,4-naphthoquinone monophenylhydrazone (existing only in the ketone-hydrazone form), Hadzi [9] found three maxima at 3340, 3240 and 3140 cm^{-1}, i.e., frequencies identical with those characteristic of the monohydrazone (I). Hadzi observed a group of bands near 2900 cm^{-1} for derivatives of 1,2-naphthoquinone that exist in tautomeric forms.

Evaluations of the absorption bands in the 1700-1400 cm^{-1} region was difficult since this region contains the frequencies of the valence vibrations of the double-bond groups (C = O, C = N), of phenyl and of the deformation vibrations of the N-H group. Possible shifts and overlapping of bands still further complicates the spectrum. We distinguished between five groups of bands with the following frequencies (cm^{-1}): 1665-1620 (ketone group), 1620-1604 (phenyl), 1600-1570 (conjugated phenyl), 1565-1540 (C = N double bond), 1500-1480 (phenyl).

The three groups of bands that we associate with the phenyl group are in accordance with literature data [10].

Bands in the 1540-1565 cm^{-1} region correspond to the C = N bond. They are observed for all of the compounds (I) to (VI) and have been accurately measured in a paper devoted to an investigation of benzil monodimethylhydrazines [11]. This band was not evaluated in Hadzi's paper [9] but is present in the spectra of all the compounds. In 1,4-naphthoquinone monohydrazone it overlaps with a strong band at 1538 cm^{-1} (C_6H_5-NH) but it stands out clearly in the deuterated derivative where the 1538 cm^{-1} band is shifted toward the lower frequencies.

The strong bands in the 1615 cm^{-1} region are associated with the ketonic group. They are absent from benzoin hydrazone (VI) and benzil dihydrazone (IV). This band, like the carbonyl group band, was identified by Hadzi [9] who found that it is absent from the spectrum of the methyl ethers of phenylazonaphthols.

On comparing the frequencies of the ketonic group in monohydrazones of dibenzosuberanedione-6,7 and in benzil with the frequency of this group in diketones, we find that the ketonic group in benzil corresponds to an absorption band at 1681 cm^{-1} (in $CHCl_3$) [12], while the isomeric monodimethylhydrazones of benzil give nearly the same vibration frequency (1661 and 1672 cm^{-1}) [11]. In the case of benzil monohydrazone (III), however, it is shifted 30 cm^{-1} toward the shorter frequencies.

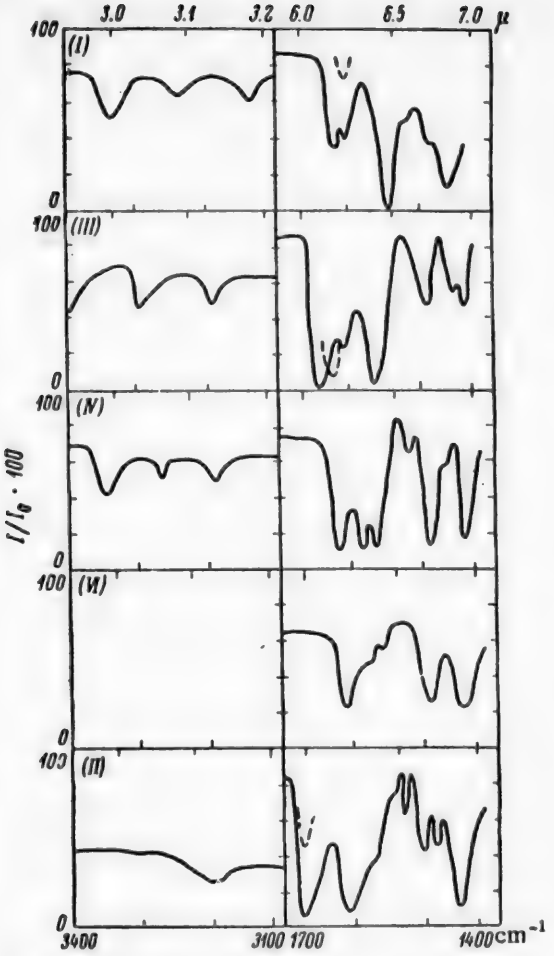
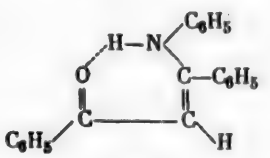


Fig. 3. Infrared absorption curves of the monohydrazone (I) and monoxime (II) of dibenzosuberanedione-6,7, monohydrazone (III) and dihydrazone (IV) of benzil, and the hydrazone (VI) of benzoin.



(VII)

Dibenzosuberanedione-6,7 has an absorption band at 1672 cm^{-1} [2] corresponding to the carbonyl groups. It retains this position in the monoxime (II) but there is a sharp shift of 50 cm^{-1} toward lower frequencies in the monohydrazone (I).

Hadzi observed a similar picture for naphthoquinone derivatives [9, 13]. 1,2-Naphthoquinone absorbs at 1657 cm^{-1}, the 2-monoxime at 1668 cm^{-1}, i.e., hardly any shift, while the 2-monophenylhydrazone absorbs at 1615 cm^{-1}, i.e., 42 cm^{-1} further into the region of shorter frequencies.

It must be emphasized that for 1,2-naphthoquinone 2-monoxime Hadzi observed a band at 3210 cm^{-1} in the OH group valence vibration region. This coincidence in OH group vibration frequencies and the absence of a ketonic band shift in 1,2-naphthoquinone 2-monoxime and dibenzosuberanedione-6,7 monoxime (II) indicate identical configurations of the two systems.

According to Palm [14] benzil α-monoxime and other α-oximes possess an OH group band close to 3250 cm^{-1}. Therefore dibenzosuberanedione-6,7 (II) has the α-(anti) configuration.

The lower frequency of vibration of the ketonic group in monohydrazones is due to the presence of a conjugated hydrogen bond (chelate ring). Investigations of the infrared spectra of α, β -unsaturated α-aminoketones (VII) by Cromwell and co-workers [15] showed that a hydrogen bond in a chelate ring lowers the vibration frequency of the ketonic group by 20-80 cm^{-1}. Conjugation has an appreciable influence in tertiary amines (40 cm^{-1} shift in this band). As the formulas show α,β -unsaturated α-aminoketone and α-diketone monohydrazone are similar in structure (the hydrazone has a nitrogen in place of carbon). In other respects they are the same; we therefore suggest that the lowering of the ketonic group frequency in monohydrazone (I) is caused by the hydrogen bond and by the conjugation of the ketonic group with the C = N double bond and the free electron pair at the nitrogen atom in the β -position. Such a conjugation diminishes the double-bond character of the ketonic group and therefore lowers the frequency.

Steric considerations can account for the different magnitudes of shift of the ketonic band in dibenzosuberanedione-6,7 (I) and benzil monohydrazone (III) and also for the absence of shift in benzil monodimethylhydrazone.

An examination of models by Leonard [2] showed that the ketonic groups in dibenzosuberanedione-6,7 have cis-position. But they are displaced from the planar position due to repulsion by the C = O dipoles. The models showed that monohydrazone (I) will have an identical structure or even one closer to planarity, for the dipole repulsion will be smaller. Such a spatial arrangement and the syn-configuration of the monohydrazone (I) create favorable conditions for conjugation and formation of a hydrogen bond, as reflected in the marked shift of the vibration frequency of the ketonic group.

TABLE 3

Name	Melting point *	
	our data	literature data
Dibenzosuberanedione-6,7 monoxime (II)	193—194°	194—195° [2]
Benzil monohydrazone (III)	146—148	147—151 [3]
Benzil dihydrazone (IV)	150—151	150—151 [4]
Benzil dihydrazone (V)	185—187	197 [5]
Benzoin hydrazone (VI)	80—82	75 [6]

* The melting points are uncorrected.

A skew configuration was assigned to benzil on the basis of x-ray structural analysis [16] and a study of the dipole moments of solutions [17]. The benzene rings and the adjacent ketone groups are in the same plane. The angle between the ketone groups is 90-100°. Conjugation of the ketonic and hydrazone groups is impossible with such a configuration, and we observe only a slight decrease in the vibration frequency of the ketonic group due to the hydrogen bond.

These views are further supported by the fact that there is hardly any shift of the absorption band of the ketonic group to lower frequencies in benzil monodimethylhydrazone which probably contains only a very weak C = O . . . H-C hydrogen bond [11].

Comparison of monohydrazone (I) with dibenzosuberanedione-6,7 monoxime (II) shows that the former compound exhibits a strong shift of the ketonic group band while no shift occurs in the latter. The absorption in the 3000 cm^{-1} region points to a syn-configuration of monohydrazone (I) (the 3140 cm^{-1} band reflects a strong, intramolecular hydrogen bond). As we already mentioned, an anti-configuration is more probable for monoxime (II); such a configuration excludes the possibility of an intramolecular hydrogen bond, and an influence on the ketone group is therefore absent.

The two compounds will also differ in the degree of conjugation of the ketonic group with the atoms of nitrogen or oxygen in the β-position. The nitrogen atom is known to be less electronegative than the oxygen atom; its unshared electron pair is more mobile and easily enters into conjugation with double bonds. The oxygen retains its electron pairs more strongly, the participation of the latter in conjugation is limited, and consequently they have no effect on the vibration frequency of the ketonic group.

EXPERIMENTAL

Dibenzosuberanedione-6,7 (I) was prepared by our earlier method [1].

For purposes of comparison several hydrazones were prepared by the literature methods. Their melting points are listed in Table 3.

Ultraviolet absorption spectra. Absorption of ultraviolet light was studied with the SF-11 spectrophotometer between 240 and 500 mμ and checked with the UM-P universal monochromator for the visible region (400-500 mμ). Measurements were carried out on all substances in solution in 95% alcohol. A solution of the benzil dihydrazone isomer with m.p. 185-187° (VI) could not be prepared due to its insolubility in alcohol. Dibenzosuberanedione (I) was also examined in solution in cyclohexane and in 0.1 N NaOH in alcohol. Its spectrum did not vary with the solvent and identical curves were obtained. The spectra are plotted in Figs. 1 and 2.

Infrared absorption spectra. Absorption curves were plotted with the help of the IKS-11 monochromatic spectrophotometer.

The region of the valence vibrations of the NH and OH groups (3100 to 3500 cm^{-1}) was examined with a LiF prism. Spectra were taken of an emulsion in vaseline oil containing 20% of the substance; width of slit 125μ, depth of layer 10μ. Absorption curves are plotted in Fig. 3. Spectra could not be obtained of solutions in CCl_4, due to insolubility of the hydrazones in CCl_4. The region of the valence vibrations of the ketonic group

(1400-1800 cm^{-1}) was examined with a NaCl prism. Spectra were taken of 2.5 or 5.0% solutions in $CHCl_3$. Width of slit 100μ, depth of layer 0.5 mm. The spectra are plotted in Fig. 3.

SUMMARY

1. A study was made of the ultraviolet and infrared absorption spectra of the monohydrazines of dibenzosuberandione and benzil, as well as of related substances.

2. The spectra show that dibenzosuberanedione-6,7 monohydrazone exists in the hydrazone form and that it is not tautomeric.

3. The infrared spectra confirm the syn-configuration of dibenzosuberanedione monohydrazine and enable the anti-configuration to be proposed for the monoxime.

4. The shift of the absorption band of the ketonic group in the monohydrazones is explained on the basis of their spatial structure and of the possible existence of a chelate ring.

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REACTION OF ISOBUTENE NITROSOCHLORIDE WITH AMINES

SYNTHESIS OF α-AMINOALDEHYDES

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No reliable and convenient methods of preparation of aliphatic α-aminoaldehydes have been reported in the literature. Some α-aminoaldehydes have been prepared (yields not stated) by the action of amines on α-haloaldehydes [1, 2], and by reduction of esters [3-5] or chlorides [6] of α-aminoacids. In the last two methods the α-aminoaldehydes were not isolated in the free state but were transformed into acetals [4] or at once employed in condensation reactions.

For this reason great interest is attached to the previously unaccomplished transition from mono-and unsymm-disubstituted olefinic hydrocarbons, via their nitrosochlorides, to α-aminoaldehydes.

In the present work we studied the reaction of isobutene nitrosochloride with a series of primary and secondary amines, leading to oximes of α-aminoaldehydes, and conversion of the latter to α-aminoaldehydes.

According to the literature trimethylethylene nitrosochloride reacted with ammonia to give 2-amino-2-methylbutanone-3 oxime [7], while under similar conditions isobutene nitrosochloride gave 2-amino-2-methylpropanal oxime [8]. A patent [9] described the preparation of a series of substitution products from isobutene nitrosochloride and secondary aliphatic amines. A study has also been made of the action of amines (mostly aromatic amines and piperidine) on nitrosochlorides of terpenic hydrocarbons, mainly with the aim of identification of terpenes [10].

We reacted isobutene nitrosochloride with methyl-, ethyl-, n-propyl-, and n-butylamine, 2-aminobutane, 2-aminohexane, benxylamine, and dimethyl- and diethylamine.• The main reaction products were oximes of α-aminoaldehydes or their salts. The general equation of the reaction is

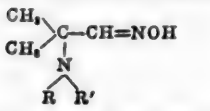
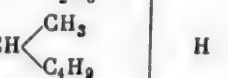
$$(C_4H_8NOCl)_2 + 2NHRR' \longrightarrow 2\ \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} NRR' \cdot HCl \\ CH{=}NOH \end{matrix}$$

The problem of the route followed by the reaction is linked to the problem of the structure of isobutene nitrosochloride. The latter has been assigned the structure of the oxime of α-chloroisobutyraldehyde [11] or of its dimer [12]. It is true that isobutene nitrosochloride does not give the Liebermann reaction for the nitroso group and does not form colorless solutions in organic solvents. On the other hand, the proposed structure as the dimer of the oxime of α-chloroisobutyraldehyde is inconsistent with the fact that oximes are usually monomolecular. The oximes of α-hydroxy-, α-methoxy-, α-ethoxy-, and α-propoxyisobutyraldehydes [13] prepared from isobutene nitrosochloride, and the oxime of 2-chloro-2-methylbutanone-3 prepared from trimethylethylene nitrosochloride [14], are also monomolecular compounds.

•An experiment with aniline gave a viscous product which could not be purified.

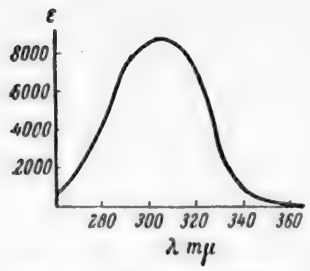
TABLE 1

Products of Reaction of Isobutene Nitrosochloride with Amines

Compound No.			Melting point	% N		Neutralization equivalent		Yield (%)•	Hydrochloride		
									melting point••	equivalent	
	R	R′		found	calculated	found	calculated			found	calculated
(I)	CH_3	H	98—99°	24.35	24.12	115.1, 116.6	116.1	81	209—210°	152.9	152.6
(II)	C_2H_5	H	108—108.5	21.62	21.53	129.5, 130.4	130.1	68	170—171	170.3	166.6
(III)	n-C_3H_7	H	78.5—79.5	19.59, 19.57	19.43	143.1, 143.2	144.2	82	178—179	177.8	180.7
(IV)	n-C_4H_9	H	70—71	—	—	158, 158.3	158.2	67	160—162	189.3	192.2
(V)		H	48—49	17.38, 17.48	17.71	158.2, 158.4	158.2	59	—	—	—
(VI)		H	51—52	14.87	15.04	185.2, 186.3	186.3	59	166—167	217.9, 222.4	222.7
(VII)	$CH_2C_6H_5$	H	126—127	14.36, 14.69	14.58	192.0, 192.6	192.3	53	187—189	228.6	228.7
(VIII)	CH_3	CH_3	95—95.5	21.33, 21.61	21.53	130.4, 131.1	130.1	58	185—186	167.3, 167.6	166.6
(IX)	C_2H_5	C_2H_5	68—69	17.65, 17.72	17.71	156.1, 159.2	158.2	70	165—167	192.2	194.7

•Calculated on the nitrosochloride.

••With decomposition.

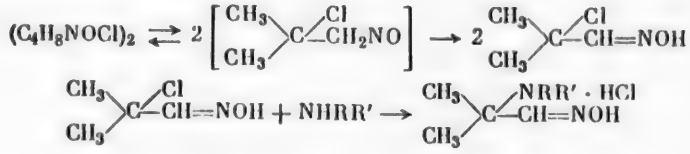


Absorption spectrum of isobutene nitrosochloride (in dioxane solution).

At the same time nearly all aliphatic C-nitroso compounds are dimers with varying degrees of stability. The electronic absorption spectrum of isobutene nitrosochloride in very dilute dioxane solution in the 270-370 mμ region (see figure) supports the view that isobutene nitrosochloride actually has the structure of a nitroso compound. The spectrum contains a well-defined absorption band with λ_{max} 307 mμ. There is a close similarity to the spectra of solutions of dimers of aliphatic C-nitroso compounds such as nitrosomethane and nitrosocyclohexane, which have precisely the same pattern of band with λ_{max} from 265 to 297 mμ and ϵ_{max} from 6000 to 10,300 [15].

We can therefore assume with a high degree of probability that isobutene nitrosochloride is the dimer of a C-nitroso compound.

Experiments on reaction of isobutene nitrosochloride with water and alcohols [13], and also experiments with amines in the present work, show that the reaction does not start immediately but after a certain period whose duration depends on the reactant, the solvent, and the temperature; it then proceeds violently with liberation of heat. This induction period may be due to the slowness of passage of the dimer into monomer, before the rapid irreversible isomerization of the monomeric nitroso compound to the chloroaldehyde oxime. Since the latter is a tertiary allylic chloride, it readily reacts exothermically with nucleophilic reagents such as water, alcohol, and amines.



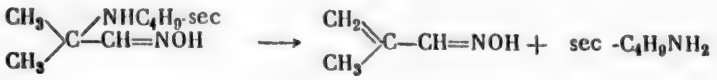
Reactions of isobutene nitrosochloride with amines were carried out in alcoholic solution. Mixtures of substitution products (oximes of α-aminoaldehydes), original amines, and their hydrochlorides were obtained in ratios depending on the type of amine and the initial proportions of reactants.

Oximes of α-aminoaldehydes are nicely crystallizing solids with a basic reaction. Their yields, physical properties, and analyses are set forth in Table 1.

Aqueous and aqueous alcoholic solutions of oximes of α-aminoaldehydes give characteristic color reactions with solutions of heavy-metal salts. With copper salts, for example, 2-methylamino-2-methylpropanal oxime (I) gives a violet color, while the remaining oximes give a dark-green color. With nickel salts all the oximes of aminoaldehydes give a color ranging from yellow to yellow-brown; oxime (I) gives a dark-red color with cobalt salts, but all the remaining compounds give dirty-green or dark-green deposits.

The presence of a secondary amine group in the products of reaction with primary amines is proven by the formation of nitrosamines on reaction with nitrous acid. Under the same conditions compounds (V), (VI), and (VII) do not give nitrosamines, due to the more rapid reaction of nitrous acid with the hydroxylamine released during acid hydrolysis of the oxime.

Synthesis of (V) was accompanied by formation of a considerable amount of 2-ethoxy-2-methylpropanal oxime due to reaction of the nitrosochloride with alcohol [13]; the oxime of methacrylaldehyde was also formed due to decomposition of (V) on heating.



The synthesized oximes of aminoaldehydes can be reduced to diamines over skeletal nickel in alcoholic solution. This reaction was carried out with (VIII).

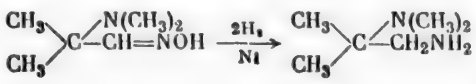
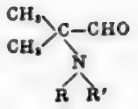


TABLE 2

α-Aminoaldehydes

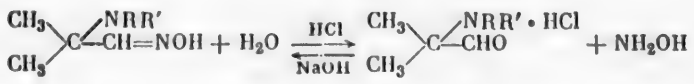


Compound No.	R	R'	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated •	Neutralization equivalent found	Neutralization equivalent calculated	Yield (%) of aldehyde	Yield (%) of dimer
(X)	CH_3	H	—	—	—	—	—	—	—	—	60
(XI)	C_2H_5	H	40°(29)	1.4532	0.9398	33.16	33.44	109.3	115.1	8	18
(XII)	n-C_3H_7	H	62—62.5 (23)	1.4561	—	—	—	129.1, 130.5	129.1	2	57
(XIII)	n-C_4H_9	H	58—62 (5)	1.4583	0.9282	42.12	42.72	140.9, 142.8	143.2	15	32
(XIV)	$CH(CH_3)(C_2H_5)$	H	65 (18)	1.4309	0.8659	42.81	42.56	146.1, 147.0	143.2	68	—
(XV)	$CH(CH_3)(C_4H_9)$	H	70 (6)	1.4364	0.8601	52.08	51.99	171.1, 172.0	171.2	33	—
(XVI)	CH_3	CH_3	57—58 (54)	1.4230	0.8817	33.27	33.58	118.5, 119.2	115.1	51	—
(XVII) ••	C_2H_5	C_2H_5	59.5 (18)	1.4311	0.8653	42.85	42.87	143.7, 144.2	143.2	67	—

•Calculated with the help of Vogel's tables of group refractions.

••According to [2]: b.p. 54° at 14 mm, n^{23} 1.4295, d^{23} 0.8618, MR 42.82.

Oximes of aminoaldehydes are easily reduced in an acid medium, but the resulting aminoaldehydes cannot be extracted from solution since they are combined as salts. Alkalization of the solution leads to instantaneous reformation of the oxime:



Sodium nitrite was added to the solution to preclude formation of oxime on alkalization. Under the conditions of hydrolysis (excess of hydrochloric acid) this step led to decomposition of the hydroxylamine.• Breakdown of hydroxylamine and alkalization were followed by extraction of the aminoaldehydes from the solution with ether. Yields of α-aminoaldehydes, their constants and analyses are presented in Table 2.

All the aminoaldehydes give a silver mirror with ammoniacal silver oxide, but do not give a cuprous oxide precipitate with Fehling solution. The presence of a carbonyl group is reflected in the infrared spectra by the appearance of a very strong absorption band in the 1720-1740 cm^{-1} region, which is characteristic of the carbonyl of aliphatic aldehydes [17]. Compounds (XV), (XVI) and (XVII) have absorption maxima at 1724, 1734 and 1727 cm^{-1}, respectively.

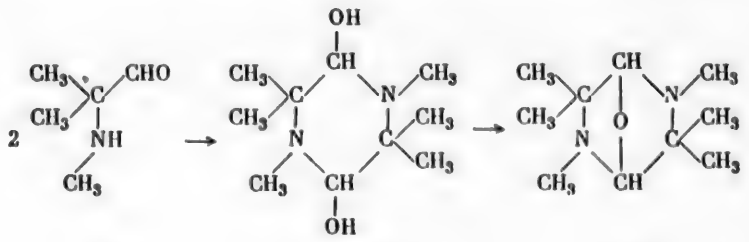
Reaction of aminoaldehydes with alcoholic hydroxylamine hydrochloride gave hydrochlorides of oximes identical with those prepared from isobutene nitrosochloride and amines.

Investigation of α-aminoaldehydes containing a primary and secondary amino group is hindered by their susceptibility to condensation. The relation between the structure of α-aminoaldehydes and this susceptibility has not previously been considered in the literature.

In our experiments secondary α-aminoaldehydes were obtained both in monomeric and dimeric forms. The ability of α-aminoaldehydes to exist in the form of monomers is markedly dependent on the structure of the radical at the nitrogen atom. Compounds containing sec -butyl (XIV) and sec -hexyl (XV) radicals were obtained in good yields and are fairly stable when stored. Their low susceptibility to condensation may be accounted for by the branched structure of the hydrocarbon radical at the nitrogen, which creates steric hindrance to interaction between the amino group and the carbonyl group.

Aminoaldehydes containing the CH_3 (X), C_2H_5 (XI), n-C_3H_7 (XII), and n-C_4H_9 (XIII) radicals were usually found to be very unstable and changed into condensation products (piperazine derivatives).

2-Methylamino-2-methylpropanal (X) was not isolated at all; only two dimers corresponding to it were obtained: crystalline 1,2,2,4,5,5-hexamethyl-3,6-dihydroxypiperazine (XVIII) (m.p. 39.5-41°) and the corresponding oxide—the liquid 1,2,2,4,5,5-hexamethyl-3,6-epoxypiperazine (XIX).

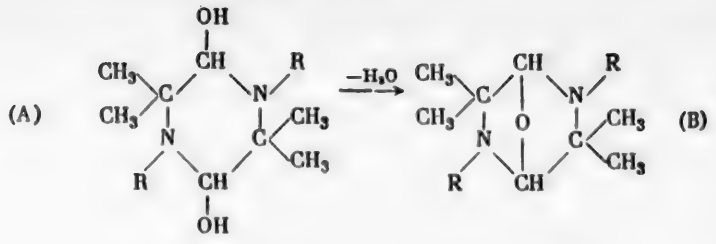


(X) (XVIII) (XIX)

Compound (XVIII) was found to split off water with great facility to form the oxide (XIX). The latter avidly takes up water with formation of a crystal hydrate $C_{10}H_{20}ON_2 \cdot 3H_2O$.

Aminoaldehydes (XI), (XII) and (XIII) were obtained in monomeric form in low yield; in these cases the main products were oxides (XX), (XXI) and (XXII), resulting from detachment of a molecule of water from the initially formed dihydroxypiperazines of the type of (XVIII) (A).

•According to the reaction $NH_2OH + HNO_2 = N_2O + 2H_2O$, see [16].



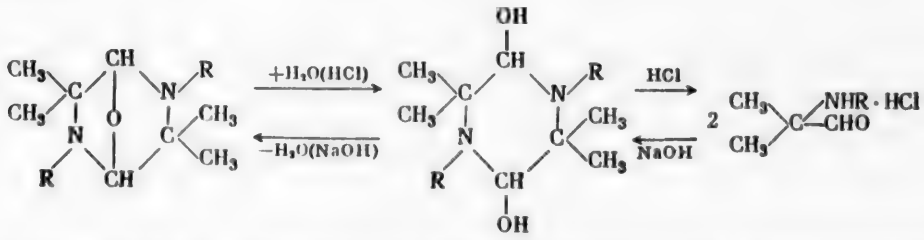
(A) (B)

For (B): R = C_2H_5 (XX), n-C_3H_7 (XXI), n-C_4H_9 (XXII).

Dimer (XVIII) partially dissociates even in benzene solution. Dimers (XIX)-(XXII) are stable when dissolved in organic solvents, but in an aqueous alkaline medium they exist (at any rate partly) in the form of monomeric aminoaldehydes.

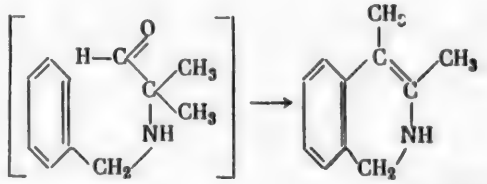
The dimers partly displace (wholly when heated) the hydrochloric acid from hydroxylamine hydrochloride in an aqueous solution neutralized with hydrochloric acid. Reaction of dimer (XXI) with alcoholic $NH_2OH \cdot HCl$ gave the aminoaldehyde oxime (III) hydrochloride, identical with that prepared from isobutene nitrosochloride and propylamine. The majority of the dimers reduce both ammoniacal silver oxide and Fehling reagent.

All these facts point to the existence of an equilibrium between the monomeric and dimeric forms of α-aminoaldehydes:



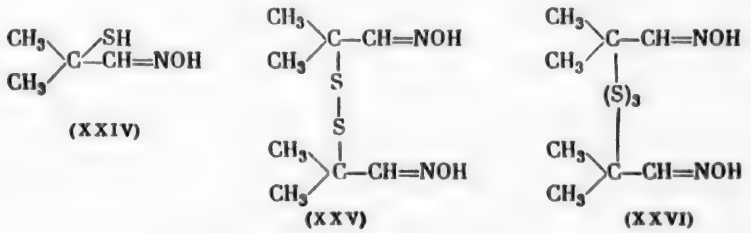
This singular type of ring–chain equilibrium resembles the equilibrium of α-hydroxyaldehydes, but an acid medium markedly influences the position of the equilibrium of α-aminoaldehydes.

Hydrolysis of the oxime of 2-benzylamino-2-methylpropanal (VII) gave a dimer of the type of the substituted dihydroxypiperazine (A). Heating of the product of hydrolysis with concentrated sulfuric acid at 180-200° gave very little base, • apparently 3,4-dimethyl-1,2-dihydroisoquinoline (XXIII); it was isolated as the picrate and methiodide:



(XXIII)

An attempt was made to prepare the oxime of α-mercaptoisobutyraldehyde. Reaction of isobutene nitrosochloride with NaHS gave, instead of the expected mercaptan (XXIV) the dioxime of 2,2'-dithio-2,2'-dimethyldipropanal (XXV) and the dioxime of 2,2'-trithio-2,2'-dimethyldipropanal (XXVI).



(XXIV) (XXV) (XXVI)

•Analogous to the formation of dihydroisoquinoline on heating of aminoacetal with sulfuric acid [18].

EXPERIMENTAL

Starting components. Isobutene was obtained by dehydration of isobutyl alcohol over activated alumina at 450-500° and was brought into reaction without further purification.

Nitrosyl chloride was prepared by reaction of sodium nitrite solution with concentrated hydrochloric acid [19]. The product was freed of HCl and oxides of nitrogen by refluxing for half an hour (30-40°); it was then distilled.

Isobutene nitrosochloride was prepared by reaction of nitrosyl chloride with excess of isobutene in ethereal solution [13]; yield 45-55%. A product with a melting point not below 98° was used without recrystallization. According to [13] it has m.p. 104°.

Methylamine, dimethylamine and ethylamine were prepared from the commercial salts of the amines by treatment with caustic alkali; they were dried with soda lime and dissolved in 95% alcohol.

Diethylamine. The commercial preparation was fractionated in a column and the 54.7-56° fraction was collected; according to [20] b.p. 55°.

Propylamine. A preparation with b.p. 46.8-49° and $n^{20}D$ 1.3882 was used.

According to [20] it has b.p. 48° (750 mm), $n^{20}D$ 1.38815.

2-Aminobutane was prepared by hydrogenation of methylethyl ketone oxime over Raney nickel in alcohol at 180° and 150-200 atm; yield 71%. 2-Aminobutane was used in alcoholic solution; it was obtained by distillation of the hydrogenation product at 60-78°. Part of the amine was purified via the hydrochloride. B.p. 62-63°, $n^{20}D$ 1.3933, d^{20}_4 0.7228.

According to [20] it has b.p. 63.5°, $n^{20}D$ 1.3932, d^{20}_4 0.7246.

2-Aminohexane was obtained by hydrogenation of 2-hexanoneoxime over Raney nickel in a little alcohol at 200° and 150-200 atm; yield 26%.

It was dried with caustic alkali and distilled in a column. B.p. 117-118°, $n^{20}D$ 1.4136, d^{20}_4 0.7637.

Literature data: b.p. 117-118°, d^{20}_0 0.7534 [21], $n^{25}D$ 1.4080 [22].

Reaction of Isobutene Nitrosochloride with Amines

Preparation of oximes of α-aminoaldehydes. An alcoholic solution of the amine was put into a flask fitted with reflux condenser, stirrer and thermometer; the finely pulverized nitrosochloride was gradually added with stirring at room temperature or with slight cooling. The reactions were exothermic. A mixture of substitution product, starting amine and their hydrochlorides was formed and was separated by the procedure given below.

The neutralization equivalents of the resulting bases were determined by titration with 0.1 N HCl in presence of bromophenol blue in water or aqueous alcoholic solution. Equivalent weights of the hydrochlorides were determined by Mohr titration (see Table 1).

Oxime of 2-methylamino-2-methylpropanal (I). A solution of 185 g of methylamine in 600 ml of alcohol was reacted with 78 g of the nitrosochloride at 18°. The alcohol boiled up and the crystals dissolved. Methylamine and alcohol were taken off in a low vacuum while heating on a water bath. Extraction of the solid residue with hot benzene gave 9 g (12%) of colorless crystals of base (I), which was purified by recrystallization from benzene. Crystallization of the benzene-insoluble residue from alcohol gave 65 g (69%) of the hydrochloride of (I), and the mother liquor containing methylamine hydrochloride was discarded.

Base (I). Found %: C 52.13; H 10.62; N 24.35. M 117.1, 112.9. $C_5H_{12}ON_2$. Calculated %: C 51.70, H 10.41; N 24.12. M 116.1.

The compound is readily soluble in water, alcohol and acetone, poorly in ether and gasoline. Does not give a precipitate of picrate in alcoholic solution.

The nitrosoamine—the oxime of 2-methylnitrosoamino-2-methylpropanal—was formed by the action of sodium nitrite solution in the cold on a hydrochloric acid solution of (I). M.p. 122.5-123° (from aqueous alcohol).

Long plates, soluble in alcohol and alkali, poorly soluble in water, ether and benzene. Gives the Liebermann reaction for the nitroso group.

Found %: N 29.16. $C_5H_{11}O_2N_3$. Calculated %: N 23.95.

Oxime of 2-ethylamino-2-methylpropanal (II). A solution of 130 g of ethylamine in 300 ml of alcohol was reacted with 81 g of nitrosochloride (ice cooling). During the reaction the temperature rose 24°. The mass was then heated to the temperature at which the precipitate dissolved (55°). After 24 hr the deposited crystals of (II) were collected (34.7 g); part of the alcohol was distilled off and a fresh crop of 23.8 g of (II) was collected on cooling. Total yield 58.5 g (68%). Purified by recrystallization from benzene.

Found %: C 55.45, 55.76; H 11.19, 11.16; N 21.62. $C_6H_{14}ON_2$. Calculated %: C 55.37; H 10.84; N 21.53.

Soluble in water, alcohol, methanol, acetone and ether; crystallizes from benzene and ethyl acetate; poorly soluble in ligroine.

Oxime of 2-propylamino-2-methylpropanal (III). Reaction between 52 g of propylamine in 75 ml of alcohol and 51.6 g of nitrosochloride was carried out as above. The cooled solution deposited 37.8 g of (III); alcohol and amine were taken off from the filtrate in vacuo, the residue was dissolved in 50 ml of water, 10 g of NaOH was added, and the liquid extracted with ether. The ether was driven off and the residue of (III) recrystallized from a mixture of benzene and ligroine (b.p. 40-60°); a further 12.4 g of (III) was obtained. Total yield 50.2 g (82%). Flat rectangular crystals. Solubility as for (II).

The hydrochloride of (III) was prepared by saturation of a benzene solution of the base with dry HCl; it was recrystallized from acetone containing a few drops of water.

Oxime of 2-dimethylamino-2-methylpropanal (VIII). A solution of 70 g of dimethylamine in 200 ml of alcohol was reacted with 37.6 g of nitrosochloride. The reaction course was the same as in the two preceding experiments. Alcohol and amine were taken off in vacuo; benzene extraction of the residue yielded 17 g of (VIII). Distillation of the benzene mother liquor in vacuo gave 1.2 g of colorless liquid with b.p. 55-63° (17 mm), $n^{20}D$ 1.478. According to [9], 2-methylpropenal oxime has b.p. 51-53° (15 mm), $n^{20}D$ 1.4789. The distillation residue contained 6.3 g of (VIII). Total yield 23.3 g (58%).

Readily soluble in water, alcohol and ether, very poorly soluble in ligroine. Picrate: m.p. 169-170° (from alcohol); yellow needles.

The hydrochloride of (VIII) was prepared by saturation of the acetone solution with dry HCl; it was recrystallized from alcohol–acetone mixture and washed with ether.

Hydrogenation of 3.3 g of (VIII) was effected in alcohol in presence of Raney nickel at atmospheric pressure. After the nickel had been separated, the solution was evaporated and saturated with dry HCl. Long needles of the dihydrochloride of 1-amino-2-dimethylamino-2-methylpropane came down on cooling. Yield 1 g (21%). M.p. 235-236° (from alcohol). Picrate, m.p. 200-201° (from alcohol); yellow needles.

Found: equiv. (Mohr's method) 92.7, 99.6. $C_6H_{18}N_2Cl_2$. Calculated: equiv. 94.6.

Oxime of 2-diethylamino-2-methylpropanal (IX). Reaction was effected between 80 g of diethylamine in 150 ml of alcohol and 67.5 g of nitrosochloride. The reaction goes slowly in the cold but is strongly exothermic at room temperature. Cooling of the solution at first down to -20° and later down to -35° led to separation of 72 g of crystals from which 45.2 g of (IX) was extracted with ether. The filtrate after the freezing-out was distilled in vacuo for removal of alcohol and amine, and the residue was combined with that from the ether extraction. The combined residues were dissolved in water and the solution was extracted with ether for removal of the oxime of 2-methylpropanal (0.9 g of the latter was isolated after the ether had been driven off). Alkali was carefully added to the aqueous solution and the precipitated flocs were extracted with ether. The ether was evaporated, and the solid residue washed with ligroine and dried in vacuo; yield 16.6 g. Total yield 61.8 g (70%). Purified by precipitation from alcoholic solution with water or by recrystallization from ligroine. Colorless crystals, readily soluble in alcohol, ether, acetone and benzene, poorly in water.

The hydrochloride of (IX) was purified by reprecipitation with ether from alcoholic solution.

Oxime of 2-n-butylamino-2-methylpropanal (IV). Prepared by the usual method from 55 g of butylamine ($n^{20}D$ 1.3931—according to [20] it has $n^{20}D$ 1.4008), 65 g of alcohol and 44 g of nitrosochloride. After the reaction mixture had cooled and stood overnight, crystals of the oxime hydrochloride came down; they were filtered, washed with a mixture of alcohol and ligroine, and dried in vacuo. Yield 23.7 g (34%).

The alcohol was distilled off from the filtrate in vacuo; the residue was heated with 30 ml of water and ether and the ether layer was separated. The aqueous solution was made alkaline and extracted with ether. The ether was driven off, and the oxime base washed with ligroine and dried in vacuo. Yield 18.6 g (33%). Total yield of oxime 42.3 g (67%). Recrystallized from benzene: flat needles with m.p. 70-71°.

Very easily soluble in alcohol, benzene, CCl_4 and ether; crystallizes from ligroine and ethyl acetate.

The hydrochloride of the oxime was recrystallized from alcohol. M.p. 160-162°.

Oxime of 2-sec-butylamino-2-methylpropanal (V). Reaction was effected between 130 g of 2-aminobutane in 180 ml of alcohol and 81 g of nitrosochloride. Procedure as above. Alcohol and amine were distilled off; the viscous residue was dissolved in 30 ml of water and 120 ml of ether; the ethereal solution was separated and dried with potassium carbonate, the ether was distilled off, and the residue mixed with three times the volume of ligroine (b.p. 60-80°). The finely crystalline precipitate was washed with ligroine and dried in vacuo; yield 45 g. M.p. 59-64°.

The ligroine was distilled off from the mother liquor and the residue distilled in vacuo to give 15 g of liquid with b.p. 54-69° at 7 mm. This was a mixture of 2-methylpropenal oxime and 2-ethoxy-2-methylpropanal oxime. The solid residue was washed with ligroine and dried in vacuo; yield 13.8 g.

The aqueous solution of salts, obtained above, was made alkaline and worked up as before to give a further 8.4 g of crystals with m.p. (from ligroine) 56-59°. Total yield of solid product 67.2 g. Compound (V) was separated from it by distillation in vacuo through a short Wurtz column without a condenser. Compound (V) at once solidified in the receiver as colorless crystals. B.p. 94.5-95.5° at 3 mm, m.p. 48-49° (without recrystallization).

Easily soluble in the majority of solvents, poorly soluble in CCl_4. Crystallizes from ligroine as soft plates with m.p. 59-60.5° (with a content of 8-10% of ligroine).

Oxime of 2-(2'-hexyl)amino-2-methylpropanal (VI). 2-Aminohexane (68 g) was reacted in alcohol (60 ml) with nitrosochloride (62 g). After the reaction, the alcohol was distilled off and 50 ml of water and ether was added to the residue to dissolve it. The ethereal solution was collected, the ether was distilled off and the residue diluted with ligroine. The hydrochloride of (VI) came down (1 g). The ligroine was taken off and the residual viscous mass distilled in vacuo from a Wurtz flask. A syrupy, colorless liquid with a faint odor was collected (16.8 g), b.p. 114-129° (4 mm). It solidified on the following day to a colorless mass. M.p. 51-52° (after freezing out from ligroine at -10°). The 114-117° fraction (4 mm) had: $n^{20}D$ 1.4679, d^{20}_4 0.9187, MR_D 56.36; calculated 56.31.

The product dissolves easily in all organic solvents and is poorly soluble in water and alkali.

Another 33 g of base (VI) was isolated from the above aqueous solution of salts by alkalization, extraction with ether and vacuum distillation. Total yield 50 g (58%).

The hydrochloride of (VI) was purified by recrystallization from acetone.

Oxime of 2-benzylamino-2-methylpropanal (VII). The reaction between benzylamine (18 g) in alcohol (15 ml) and nitrosochloride (9 g) was strongly exothermic. The cooled reaction mass deposited a mixture of (VII) and benzylamine hydrochloride. Extraction of the precipitate with benzene gave 7.5 g of (VII). Recrystallized from benzene or alcohol.

Found %: C 69.04, 68.73; H 8.57, 8.60; N 14.36, 14.69. $C_{11}H_{16}ON_2$. Calculated %: C 68.71; H 8.39; N 14.58.

Readily soluble in acetone, poorly in water and ligroine, slightly in ether; crystallines from methanol, ethyl acetate and CCl_4.

The hydrochloride of (VII) was obtained by dissolving (VII) in alcoholic HCl and was brought down from solution with ether.

Preparation of α-Aminoaldehydes

Hydrolysis of oximes of α-aminoaldehydes. The oxime and concentrated hydrochloric acid (3 moles HCl per mole oxime) were put into a flask fitted with stirrer, reflux condenser, thermometer and dropping funnel (the stem of the latter extended into the layer of liquid). A small excess (relative to the oxime) of saturated aqueous sodium nitrite was run in at 70-80° from the dropping funnel at such a rate that brown vapors of oxides of nitrogen were not evolved.

The cooled solution was extracted with ether for removal of traces of nitrosoamine and neutralized with the calculated amount of caustic alkali (or alkali + sodium carbonate); the separating base was extracted with ether and the ether taken off in vacuo without heating (the ethereal solution was not usually dried); the residue was distilled in vacuo, sometimes with addition of a few milliliters of benzene.

Neutralization equivalents of the prepared bases were determined by titration with 0.1 N HCl in presence of bromophenol blue (see Table 2). The carbonyl group content was determined in a neutralized sample by the hydroxylamine method with heating [23].

2-Dimethylamino-2-methylpropanal (XVI). From 35 g of (VIII) was obtained 14.35 g of substance with b.p. 52-54° (45 mm). Redistillation gave 11.9 g of (XVI) with b.p. 57-58° (54 mm).

Found %: N 12.19; CO 23.1. $C_6H_{13}ON$. Calculated %: N 12.16; CO 24.3.

A colorless liquid with an ammoniacal odor, turning yellow on standing, fairly soluble in water, soluble in organic solvents. Gives a violet color with aqueous $CuSO_4$. With saturated alcoholic picric acid it gives a yellow precipitate that dissolves completely on shaking. Passage of dry HCl into a benzene solution of (XVI) leads at first to precipitation of colorless salt but later the solution turns yellow and the precipitate dissolves. The hydrochloride of (XVI) forms hygroscopic crystals deliquescing in the air. The aminoaldehyde gives a superb silver mirror but does not give the Fehling reaction.

The oxime was obtained in the form of the hydrochloride on reaction of (XVI) with saturated alcoholic hydroxylamine hydrochloride. M.p. 182-183° (with decomp., from alcohol); equiv. wt. 166.3, calc. 166.6. No melting point depression in admixture with the hydrochloride of (VIII).

2-Diethylamino-2-methylpropanal (XVII). From 37 g of (IX) was obtained 22.2 g of substance with b.p. 57-60° (18 mm). The fraction with b.p. 59.5° (18 mm) was analyzed (weight of fraction 12.3 g).

Found %: N 9.94; CO 19.85. $C_8H_{17}ON$. Calculated %: N 9.78; CO 19.56.

A colorless liquid with an amine odor, turning yellow on standing. The oxime was obtained by the preceding method in the form of the hydrochloride, m.p. 165-167°; equiv. wt. 192.4, calc. 194.7. No depression of melting point in admixture with the hydrochloride of (IX).

2-Sec-butylamino-2-methylpropanal (XIX). From 30 g of (V) was obtained 18.5 g of substance with b.p. 63-65° at 16 mm. The residue from distillation was 3.3 g of brown mass. Redistillation gave a number of fractions boiling in the same temperature range but differing slightly in density; the middle fraction with b.p. 65° (18 mm) was analyzed (weight of fraction 4.25 g).

Found %: N 10.04; CO 18.84. $C_8H_{17}ON$. Calculated %: N 9.78; CO 19.56.

A colorless liquid with an odor of amines and camphor. The less pure fractions very quickly turned green and then became yellow after a week. The pure fractions slowly turned yellow on standing. The compound released a little water on standing in the air or in an ampoule under nitrogen, probably due to condensation.

The oxime was prepared by reaction with alcoholic hydroxylamine hydrochloride. M.p. 59-60° (from ligroine). No depression of melting point in admixture with an authentic specimen.

2-(2'-Hexyl)-amino-2-methylpropanal (XV). From 12 g of (VI) was obtained 3.6 g of substance with b.p. 69-79° (6 mm). The residue was 3.6 g of mobile brown liquid which on distillation yielded 2 g of 121-122° (5 mm) fraction, $n^{20}D$ 1.4652. The last fraction was possibly the dimer of the aminoaldehyde; the fraction became heterogeneous on standing and therefore was not analyzed.

Found for the 70° (6 mm) fraction (1.5 g), %: CO 16.31. $C_{10}H_{21}ON$. Calculated %: CO 16.37.

A colorless liquid with a characteristic odor, rapidly turning yellow on standing (less pure fractions very quickly turned green). A blue-violet precipitate was obtained with solutions of copper salts.

Hydrolysis of the oxime of 2-methylamino-2-methylpropanal (I). Hydrolysis of (I) (45 g) was carried out as above. After the ether had been taken off, 5.7 g of colorless liquid was distilled in vacuo from a Claisen flask; b.p. 72° (43 mm); the product solidified in the condenser and receiver to a colorless crystalline mass (XVIII). The residue was distilled from a Wurtz flask with a low side-tube; 13.5 g of liquid with b.p. 56-80° (15 mm) was collected; residue 6.7 g.

Compound (XVIII) was dried on a porous plate in the air. M.p. 39.5-41°. It formed a silver mirror and gave a Fehling reaction. Water is very easily lost on heating with solvents or during drying in vacuo, with transformation into liquid product (XIX) (see below). A progressive increase in depression is observed during molecular weight determination. A light-violet color develops with solutions of copper salts.

Found %: N 13.27, 13.34; CO 27.40. No. H_{act} 2.17. M 206.0. Equiv. 101.0, 102.3. $C_{10}H_{22}O_2N_2$. Calculated %: N 13.85; CO 27.7 (calculated for two carbonyl groups in the molecule). M 202.3. Equiv. 101.1. No. H_{act} 2.00.

Compound (XVIII) was the dimer of aminoaldehyde (X)—1,2,2,4,5,5-hexamethyl-3,6-dihydroxypiperazine.

Several fractionations of the liquid with b.p. 56-80° (15 mm) gave a series of fractions that wholly or partly solidified to crystals identical with (XVIII). In addition 2 g of (XIX) was collected—a colorless, viscous liquid with a faint amine odor, avidly absorbing moisture from the air. It reduced Fehling solution and gave a silver mirror.

B.p. 77.5-79.5° (13 mm), $n^{20}D$ 1.4571, d^{20}_4 0.9682, MR_D 51.84; calculated 53.50.

Found %: CO 29.7. M 182.5, 187.9. Equiv. 91.4, 91.6. $C_{10}H_{20}ON_2$. Calculated %: CO 30.2 (calculated for two carbonyls in the molecule). M 184.3. Equiv. 92.1.

Compound (XIX) is 1,2,2,4,5,5-hexamethyl-3,6-epoxypiperazine.

Heat was released when (XIX) was shaken with water and a precipitate came down which crystallized from water in the form of stout, colorless prisms. M.p. 67-70° after washing with ether and drying in the air. Gave a silver mirror and a positive Fehling reaction. The product was the trihydrate of oxide (XIX).

Found %: CO 23.26. Number of molecules of water 3.10, 2.86. Equiv. 118.1, 120.1. $C_{10}H_{20}ON_2 \cdot 3H_2O$ Calculated %: CO 23.48. Number of molecules of water 3.00. Equiv. 119.1.

Hydrolysis of oxime of 2-ethylamino-2-methylpropanal (II). The ethereal solution of the products of hydrolysis of (II) (30 g), obtained as described above, was dried for three days with sodium sulfate, the ether was driven off, and the residue distilled in vacuo to give 1.1 g of substance with b.p. 40-50° (29 mm). The compound was evidently 2-ethylamino-2-methylpropanal (XI). The 40° (29 mm) fraction (0.6 g) was analyzed (see Table 2). A liquid with an amine odor, slightly soluble in water, gives a bright-blue coloration with solutions of copper salts. Gives a silver mirror but does not reduce Fehling reagent.

Further fractionation of the products of hydrolysis of (II) gave a substance with b.p. 68-70° (10 mm) which solidified to crystals in the condenser. Vacuum sublimation of the residue yielded a further crop of colorless crystals. After drying on a porous plate the total yield was 4 g. B.p. 42-43°. Readily soluble in alcohol and ether, poorly soluble in water; does not contain active hydrogen.

Found %: CO 26.65. M 213.6, 211.4. Equiv. 105.4, 105.8. $C_{12}H_{24}ON_2$. Calculated %: CO 26.4 (two carbonyls in the molecule). M 212.3. Equiv. 106.1.

The substance was 2,2,5,5-tetramethyl-1,4-diethyl-3,6-epoxypiperazine (XX).

Hydrolysis of the oxime of 2-propylamino-2-methylpropanal (III). From 36 g of (III) was obtained 0.3 g of 62-62.5° (23 mm) fraction corresponding to 2-propylamino-2-methylpropanal (XII) (see Table 2). A compound with an amine odor, turning yellow on standing. It gives a silver mirror but does not reduce Fehling reagent. It gives a blue-violet color with solutions of copper salts. The carbonyl group content could not be determined by the hydroxylamine method.

Distillation of the products of hydrolysis of (III) also gave 17 g of a substance with b.p. 89-98° (3 mm). The residue was 8 g of brown liquid.

The 89-98° (3 mm) fraction was redistilled.

B.p. 95-95.5° (3 mm), $n^{20}D$ 1.4577, d^{20}_4 0.9266, MR_D 70.71; calc. 71.97.

Found %: N 11.44, 11.55. M 224. $C_{14}H_{28}ON_2$. Calculated %: N 11.66. M 240.

Nearly colorless, mobile liquid with a weak odor. Gives a silver mirror and Fehling reaction. Does not contain active hydrogen. Consistent results are not obtained in determinations of the neutralization equivalent. The substance is 2,2,5,5-tetramethyl-1,4-dipropyl-3,6-epoxypiperazine (XXI). The latter was heated with alcoholic hydroxylamine hydrochloride. Crystals came down on cooling and were recrystallized from acetone containing a few drops of water. M.p. 178-178.5°. No depression of melting point in admixture with the hydrochloride of (III).

Hydrolysis of the oxime of 2-n-butylamino-2-methylpropanal (IV). Hydrolysis of 30.3 g of the oxime was effected in the usual manner. After removal of the ether, 4.1 g (15%) of aldehyde fraction with b.p. 58-62° (5 mm) was collected.

A colorless liquid with a characteristic burned smell. The compound turns yellow on standing, and the neutralization equivalent increases. In addition to the aldehyde fraction, there was isolated a fraction that appeared to be its dimer. B.p. 112-122°, yield 8 g (32%), $n^{20}D$ 1.4612. The fractionation residue was 10 g of heterogeneous brown mass. The two fractions (monomer and dimer) give a silver mirror but do not reduce Fehling reagent.

Hydrolysis of the oxime of 2-benzylamino-2-methylpropanal (VII). a) 23.8 g of (VII) was hydrolyzed in the usual manner. Alkalization resulted in separation of an oil which changed to a brown resin after a few minutes, insoluble in ether and benzene. The product was heated with excess concentrated sulfuric acid on an oil bath for 40 min at 180-200°. • After cooling, the reaction mixture was poured onto ice, diluted with water, neutralized with alkali and extracted with ether. After the ether had been driven off, there was a residue of about 0.5 ml of liquid from which could be distilled a few drops of reddish liquid with a quinolinic odor and boiling above 250°. It was apparently 3,4-dimethyl-1,2-dihydroisoquinoline (XXIII).

The picrate was very poorly soluble in alcohol. M.p. 212-213° (from glacial acetic acid); greenish-yellow needles.

Found %: N 14.79, 14.85. $C_{17}H_{16}O_7N_4$. Calculated %: N 14.43.

The methoidide was obtained when (XXIII) was stood with CH_3I in ethereal solution; it was recrystallized from alcohol. A yellowish powder, turning brown and decomposing above 160° without melting.

Found: equiv. weight (Mohr) 317.7, 321.5. $C_{13}H_{18}NI$. Calculated: equiv. weight 315.1.

b) Hydrolysis of (VII) (9.3 g) was carried out in the usual manner, but the compound was treated with a deficiency of alkali in presence of ether and the ether layer was quickly separated. After a day the ether solution deposited large crystals which were washed with ether and dried in vacuo. Yield 4.3 g, m.p. 114.5-115.5°. Gives a silver mirror but does not reduce Fehling reagent.

Found %: CO 16.08. M 324. Equiv. 177.2, 180.3. $C_{22}H_{30}O_2N_2$. Calculated %: CO 15.80. M 354.5. Equiv. 177.2.

The compound is probably 2,2,5,5-tetramethyl-1,4-dibenzyl-3,6-dihydroxypiperazine.

Reaction of Isobutene Nitrosochloride with Sodium Hydrosulfide in Alcoholic Solution

An alcoholic solution of NaHS was prepared by saturation of a solution of 46 g of sodium in 650 ml of 95% alcohol with dry hydrogen sulfide. To the solution was added 78.5 g of nitrosochloride in the usual manner. Since the reaction went very slowly at room temperature, the flask was heated on a bath with a temperature of 37°; subsequently the temperature in the flask rose spontaneously to 58°. The solution was was further heated for half an

• Evolution of SO_2 was not observed during heating.

hour at 60°; the cooled solution was filtered from NaCl and the alcohol was taken off in vacuo. During the course of distillation a viscous deposit (product C) was twice suction-filtered; finally the alcohol was completely distilled and left a residue (D).

Product C and the NaCl were worked up together with water and ether; the ethereal layer was separated and the ether evaporated. Prismatic crystals of (XXV) came down from the residue. Yield 7.6 g (10%). M.p. 131.5-132° (from alcohol).

The compound crystallizes from alcohol in the form of transparent prisms, and from water and aqueous alcohol in the form of dendrites. Insoluble in benzene and ligroine, readily soluble in alcohol and acetone, poorly in hot water and CCl_4. Does not give a positive reaction for mercaptans [24]. Gives a reddish-brown precipitate after standing with copper salts. It gives a positive reaction for oxime and reduces Fehling reagent after boiling with acid.

Found %: N 11.76, 11.76; S 27.08, 26.99. M 238.1, 229.6• $C_8H_{16}O_2N_2S_2$. Calculated %: N 11.85; S 27.13. M 236.4.

The compound is the dioxime of 2,2'-dithio-2,2'-dimethyldipropanal (XXV).

Product D was dissolved in water and combined with the aqueous solution obtained by treatment of C; the solution was acidified with concentrated hydrochloric acid until acid to litmus and extracted with ether. The ether was driven off, the viscous residue extracted with benzene,•• and the insoluble precipitate separated. Weight 14.1 g (16%) after washing with benzene and drying in vacuo. M.p. 149.5-150.5° (from aqueous alcohol or aqueous acetone); colorless rod-like crystals. Insoluble in water, benzene and ligroine, readily soluble in alcohol and acetone. Does not give a positive test for mercaptans. Gives a reddish-brown precipitate with copper salts on standing. Gives a qualitative reaction for an oxime.

Found %: N 9.91, 9.93; S 33.11, 33.29. $C_8H_{16}O_2N_2S_3$. Calculated %: N 10.51; S 35.84. $C_8H_{16}O_2N_2S_3 \cdot H_2O$. Calculated %: N 9.84; S 33.59.

The compound is the dioxime of 2,2'-trithio-2,2'-dimethyldipropanal (XXVI), apparently containing a molecule of water.

SUMMARY

1. Isobutene nitrosochloride was reacted with nine primary and secondary amines of the aliphatic series. It was shown that the main products of the reactions are oximes of 2-alkylamino- and 2-dialkylamino-2-methylpropanals.

Reaction with sodium hydrosulfide gave dioximes of dithio- and trithioaldehydes.

2. Hydrolysis of the various oximes gave 33 to 68% yields of α-aminoaldehydes: 2-diethylamino-, 2-dimethylamino-, 2-sec-butylamino-, and 2-(2'-hexyl)amino-2-methylpropanals.

3. The main products of hydrolysis of oximes of 2-methylamino-, 2-ethylamino-, 2-propylamino-, 2-butylamino-, and 2-benzylamino-2-methylpropanals were dimers of α-aminoaldehydes to which were assigned cyclic structure. Secondary products (in small yield) of hydrolysis of oximes of 2-ethylamino-, 2-propylamino-, and 2-butylamino-2-methylpropanals were the corresponding α-aminoaldehydes.

4. It was shown that the stability of α-aminoaldehydes containing a secondary amino group depends mainly on the structure of the hydrocarbon radical at the nitrogen atom: Stable compounds are α-aminoaldehydes with a branched radical at the nitrogen atom, starting from the sec-butyl radical.

5. Considerations in support of the hypothesis that isobutene nitrosochloride has the structure of a dimeric nitroso compound are discussed.

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REACTIONS OF AMINES WITH HALOGEN COMPOUNDS

I. REACTION OF 1,2-DIBROMOCYCLOHEXANE WITH ANILINE, METHYLANILINE AND ETHYLANILINE

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A. E. Favorskii showed that caustic alkali can split off two atoms of halogen from polyhalogen derivatives of the aliphatic [1] and alicyclic [2] series. Subsequent investigations by many chemists also established the ability of organic bases (such as quinoline) to split off from halogenated alicyclic compounds not only the elements of hydrogen halides but also halogens. The products of reaction of quinoline with 1,2-dibromocyclohexane, for example, included cyclohexene and 1,3-cyclohexadiene [7-8]. A. E. Favorskii made a close study of the problem of the cleaving action of alkalies and quinoline and attempted to explain the observed anomalies in these reactions by stereochemical considerations [3]. Later examination of the products of reaction of quinoline with 1,2-dibromocyclohexane revealed the presence of benzene [10-13] in addition to cyclohexene and 1,3-cyclohexadiene. Similar observations were made for the reactions of homologs of 1,2-dibromocyclohexane [14] and 1-chloro-1,2-dibromocyclohexane [15]. The most interesting feature of these transformations is the formation of aromatic compounds and of cycloalkenes. Several publications have dealt with the conditions of these reactions and their mechanism [12, 14-16], with reference to the action of quinoline on halogenated compounds of the cyclohexane series.

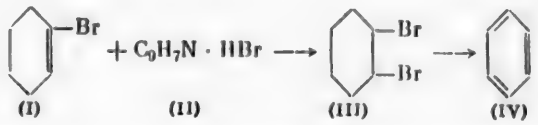
We were interested in establishing whether organic bases other than quinoline are capable of splitting off the elements of hydrogen halides as well as halogen atoms, also in establishing whether aromatization of the cyclohexane ring is specific to quinoline or whether other bases can act similarly. With these objectives we studied the interaction of 1,2-dibromocyclohexane with aniline and methyl- and ethylanilines.

Reaction of 1,2-dibromocyclohexane with methylaniline gave two fractions. One comprised cyclohexane, benzene and a small quantity of 1,3-cyclohexadiene. Its bromine number, determined by the McIlhiney method [17], was 99 (the value for cyclohexene is 195 and for 1,3-cyclohexadiene 200, assuming as repeatedly reported [7, 9, 18, 19] that 1,3-cyclohexadiene easily combines only with one molecule of bromine). The ultraviolet absorption spectrum of an alcoholic solution of this fraction contained absorption maxima at 242.5, 248.5, 254 and 261 mμ, which are characteristic of benzene. The second fraction with b.p. 162-163° was an unsaturated monobromo compound. It was of particular interest to elucidate the structure of this monobromo compound and to establish thereby the sequence of cleavage of one molecule of hydrogen bromide from 1,2-dibromocyclohexane under the action of methylaniline.

According to N. D. Zelinskii and A. I. Gorski [7], 1-bromocyclohexene-1 is formed in 15-20% yield when 1,2-dibromocyclohexane is heated with quinoline. The authors assigned this structure to the product because it was unchanged on distillation with quinoline and gave adipic acid on oxidation. The bromo compound reacted slowly with bromine in chloroform solution and hydrogen bromide was released. On the other hand Willstatter and Hatt obtained a monobromo fraction which they regarded as a mixture in view of its behavior with quinoline [10].

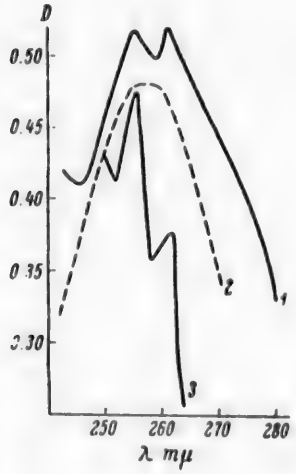
The possibility that 1,2-dibromocyclohexane can split out hydrogen bromide with formation of 3-bromocyclohexene-1 (or the corresponding ethoxy derivative) is supported by experimental work [9, 20, 21] and stereochemical considerations [3, 21, 22]. Analysis of our monobromide fraction showed it to be a mixture of 3-bromocyclohexene-1 and 1-bromocyclohexene-1. Its bromine number was 55 (the value calculated for bromocyclohexane is 99), and 3-bromocyclohexene-1 easily adds on one molecule of bromine [21, 23] while 1-bromocyclohexene-1 adds on bromine very slowly [7]. Judging by the bromine number, our mixture contains approximately 50% of 3-bromocyclohexene-1.

The action of quinoline on this monobromide fraction was also studied. This reaction gave, apart from a hydrocarbon portion, a monobromide fraction which only turned slightly cloudy with alcoholic silver nitrate, whereas the original monobromide fraction gave a voluminous precipitate. These facts indicate that the high-boiling fraction resulting from the action of methylaniline on 1,2-dibromocyclohexane contains both 3-bromocyclohexene-1 and 1-bromocyclohexene-1, and that consequently the removal by methylaniline of the elements of one molecule of hydrogen bromide from 1,2-dibromocyclohexane can proceed by two routes. The infrared absorption spectrum also contains evidence of the presence of both of the isomeric monobromides. The composition of the hydrocarbon fraction was unexpected. Apart from 1,3-cyclohexadiene this fraction also contained benzene. The mechanism of formation of the latter is still obscure. One of the possible mechanisms is the following.*



(I) (II) (III) (IV)

Favorskii [24] and Kucherov [25] had already suggested that at temperatures above 100° hydrohalides of quinoline can easily dissociate into free quinoline and hydrogen halide. On the other hand Goering [26] showed that 1-bromocyclohexene-1 in pentane adds on hydrogen bromide with formation of 1,2-dibromocyclohexane. If under our reaction conditions on interaction of the monobromide fraction with quinoline, 1,2-dibromocyclohexane can be formed from 1-bromocyclohexene-1 and quinoline hydrobromide, the formation of benzene by interaction of 1,2-dibromocyclohexane with quinoline might be represented as proceeding according to the scheme proposed by N. A. Domnin [16]. Benzene formation might also be accounted for on the assumption that quinoline N-bromides are capable of bromination in the allyl position. They are known to act on certain aromatic compounds with formation of the corresponding halogenated aromatic derivatives [31].



Absorption spectra of alcoholic solutions of hydrocarbon fractions obtained on reaction of 1,2-dibromocyclohexane with amines. 1) With ethylaniline (method b); 2) with ethylaniline (method a). Concentration of hydrocarbon fraction 0.01 wt. %; 3) with aniline. Concentration of hydrocarbon fraction 0.1 wt. %.

Heating of 1,2-dibromocyclohexane with ethylaniline also gave a hydrocarbon fraction and a monobromide fraction. The hydrocarbon fraction (1st) contained cyclohexene, 1,3-cyclohexadiene and an even larger quantity of benzene than in the former case (established by spectral measurements as shown by curve 1 in the diagram). The 1,3-cyclohexadiene content is small, judging by the fact that hydrogenation of this fraction consumed 12% more hydrogen than was calculated for cyclohexene. The 2nd fraction was a mixture of 3-bromocyclohexene-1 and 1-bromocyclohexene-1.

Gentle heating of 1,2-dibromocyclohexane with aniline (until crystals came down) gave a nearly quantitative yield of aniline hydrobromide and only a monobromide fraction. If, however, heating was continued after formation of the aniline salt, then in addition to the monobromide a

*Salt (II) is formed by interaction of quinoline with 3-bromocyclohexene-1 present in the mixture of monobromides.

Characteristics of Hydrocarbon and Monobromide Fractions Obtained by Action of Quinoline, Aniline, Methylaniline and Ethylaniline on 1,2-Dibromocyclohexane

Base	Yield (in %)		Hydrocarbon fraction	
	of monobromide fraction	of hydrocarbon fraction	bromine No.	unsaturates content
Quinoline	15-20 [7]	47 [13]	165 [12]	85 [13]
		70-75 [10]	–	86 [10]
		79 [27]	–	80-90 [12]
Aniline	12	14	120	62
Methylaniline	17	35	99	50
Ethylaniline	22	18	28	14

hydrocarbon fraction was obtained with a bromine number of 120 (diagram, curve 3). The monobromide fraction contained 3-bromocyclohexene-1 and 1-bromocyclohexene-1.

Thus the action on 1,2-dibromocyclohexane of any of the above amines does not give any single product. In all cases the reaction mixture consists of cyclohexene, 1,3-cyclohexadiene, 1-bromocyclohexene-1 and 3-bromocyclohexene-1. In addition, with any of these three amines 1,2-dibromocyclohexane is partly converted to benzene. In the past the formation of benzene has been observed only when quinoline acts on this bromo compound [10-13] (see table).

EXPERIMENTAL

1,2-Dibromocyclohexane was obtained from cyclohexane by the method of [28]. The bromide and amines were freshly distilled.

1. Reaction of 1,2-dibromocyclohexane with methylaniline. A mixture of 21.8 g of methylaniline and 39.5 g of 1,2-dibromocyclohexane was refluxed on an oil bath at 180-195° until a voluminous condensate was obtained. A fraction boiling up to 165° was then distilled off from the reaction mixture. The fraction was washed with sulfuric acid and water, dried with calcium chloride and fractionally distilled. Two fractions were collected:

1st, b.p. 80-82° (35%), $n^{20}D$ 1.4650, McIlhiney bromine number [17] 99; 2nd, b.p. 162-163° (17%), $n^{20}D$ 1.5072, d^{20}_4 1.3792, MR_D 34.7, calc. 35.0.

Found %: Br 49.2; bromine number 53. C_6H_9Br. Calculated %: Br 49.6; bromine number 99.

Strong absorption bands were found in the infrared absorption spectrum (taken with the IKS-11 apparatus) at 689, 730, 989 and 1332 cm^{-1} [29].

Reaction of the 162-163° fraction with quinoline. 9 g of freshly distilled quinoline and 6.8 g of 162-163° fraction (the absence of 1,3-cyclohexadiene was established by inspection of the ultraviolet absorption spectrum beforehand) were mixed in the cold and then heated in a Wurtz flask. After appropriate treatment of the distilled products, two fractions were obtained by fractionation. The first fraction—82.5-84.5° (25%)—had a bromine number of 142 and its ultraviolet absorption spectrum in alcohol solution (taken with the ISP-22 apparatus) established the presence of 1,3-cyclohexadiene and benzene. The second fraction had:

B.p. 160-162°, $n^{20}D$ 1.5121, d^{20}_4 1.3841, MR_D 34.6; calc. 35.0.

Found %: Br (Schultze determination) 39.36. C_6H_9Br. Calculated %: Br 49.6.

2. Reaction of 1,2-dibromocyclohexane with ethylaniline. a) A mixture of 54 g of 1,2-dibromocyclohexane and 30 g of ethylaniline was refluxed on an oil bath at 150-155°. After a voluminous condensate had

been formed, heating was continued for another 30 min. The thick, oily portion was separated, acidified with dilute hydrochloric acid and treated with steam. The residual crystals were washed several times with alcohol on a porous plate; m.p. 162-163°. The m.p. of ethylaniline hydrobromide is given as 164-166° [30]. The molecular weight of the crystalline product was determined by titration with alkali.

Found: M 206.5. $C_6H_5NHC_2H_5 \cdot HBr$. Calculated: M 203.

Steam distillation gave an oily product fromwhich was isolated a fraction with b.p. 80-83° (8.5%) (see diagram, curve 2) and a fraction with b.p. 74° (25 mm) (32%).

b) A mixture of 90 g of 1,2-dibromocyclohexane and 49.6 g of ethylaniline was refluxed for 2 hr at 155-160° on an oil bath. After cooling, the reaction mass was treated with steam to give three fractions: 1st, b.p. 80-85° with bromine number 28. The ultraviolet absorption spectrum of a 0.01% alcoholic solution of this fraction was taken with the SF-11 instrument (see diagram, curve 1). Hydrogenation of 2.3885 g of this fraction consumed 112 ml of hydrogen (platinum black, ethyl alcohol) instead of the theoretical requirement of 98 ml, i.e., 14% more than calculated for pure cyclohexene. We can therefore infer that the hydrocarbon fraction resulting from reaction of ethylaniline with 1,2-dibromocyclohexane contains 7-10% of 1,3-cyclohexadiene. The 2nd fraction had b.p. 162-166°, $n^{20}D$ 1.5010 and gave a precipitate with alcoholic silver nitrate.

Found % Br (Schultze) 42.3. M 158.6. C_6H_9Br. Calculated % Br 49.6. M 161.

Reaction of 162-163° fraction with quinoline. Reaction of 10 g of freshly distilled quinoline with 12 g of this fraction gave the following fractions: 1st, with b.p. 82-84° (53.5%), bromine number 155. The presence of benzene and 1,3-cyclohexadiene was established by the ultraviolet spectrum (ISP-22 instrument). Hydrogenation consumed 409.9 ml of hydrogen (platinum black, ethyl alcohol) instead of 329.6 ml, or 115% of the quantity calculated for cyclohexene. 2nd, b.p. 160-162° (27.5%). The infrared absorption spectrum (taken with the IKS-11 instrument) had strong bands at 690, 884, 988 and 1251 cm^{-1}.

3. Reaction of 1,2-dibromocyclohexane with aniline. a) A mixture of 55 g of 1,2-dibromocyclohexane and 24 g of aniline was refluxed until crystals of aniline hydrobromide appeared. The yield of the latter was ~90%; it was identified by analysis and mixed melting test. Distillation of the filtrate (strongly resinifying) with steam gave an oil heavier than water. This was worked up to give a fraction with b.p. 162-163° (5 mm), $n^{20}D$ 1.5018. It gave a precipitate with silver nitrate in alcoholic solution.

Found % Br (Korshun method) 49.34. M (cryoscopic) 164. C_6H_9Br. Calculated % Br 49.6. M 161.

b) Aniline (24 g) was heated to 155° and dropwise addition was made of 1,2-dibromocyclohexane (49 g). Fractional distillation gave two fractions: 1st, b.p. 79-83° (14.4%), bromine number 120 (see diagram, curve 3). Hydrogenation consumed 20% more hydrogen than the quantity calculated on the assumption that cyclohexene was the sole unsaturated hydrocarbon in this fraction. The 2nd fraction had b.p. 159-161° (12%).

Found % Br (Korshun method) 49.2. C_6H_9Br. Calculated % 49.6.

The infrared spectrum (taken with the IKS-11 instrument) contained strong absorption bands at 689, 730, 989 and 1332 cm^{-1}.

SUMMARY

1. The interaction of 1,2-dibromocyclohexane with aniline, methylaniline and ethylaniline was investigated. These amines were found capable of splitting off the elements of hydrogen bromide as well as two atoms of bromine from 1,2-dibromocyclohexane with formation of cyclohexene, 1,3-cyclohexadiene, 1-bromocyclohexene-1 and 3-bromocyclohexene-1.

2. It was established that 1,2-dibromocyclohexane is partly converted to benzene under the action of the above amines.

3. It was shown that quinoline acts on a mixture of 3-bromocyclohexene-1 and 1-bromocyclohexene-1 to give not only 1,3-cyclohexadiene but also benzene. A mechanism for the formation of benzene is put forward.

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STEREOCHEMISTRY OF NITROGEN HETEROCYCLES

VII. PREPARATION OF CIS- AND TRANS-ISOMERS OF 2,5-DIMETHYLPIPERIDINE AND THEIR CRYSTALLINE COMPOUNDS WITH ZINC CHLORIDE

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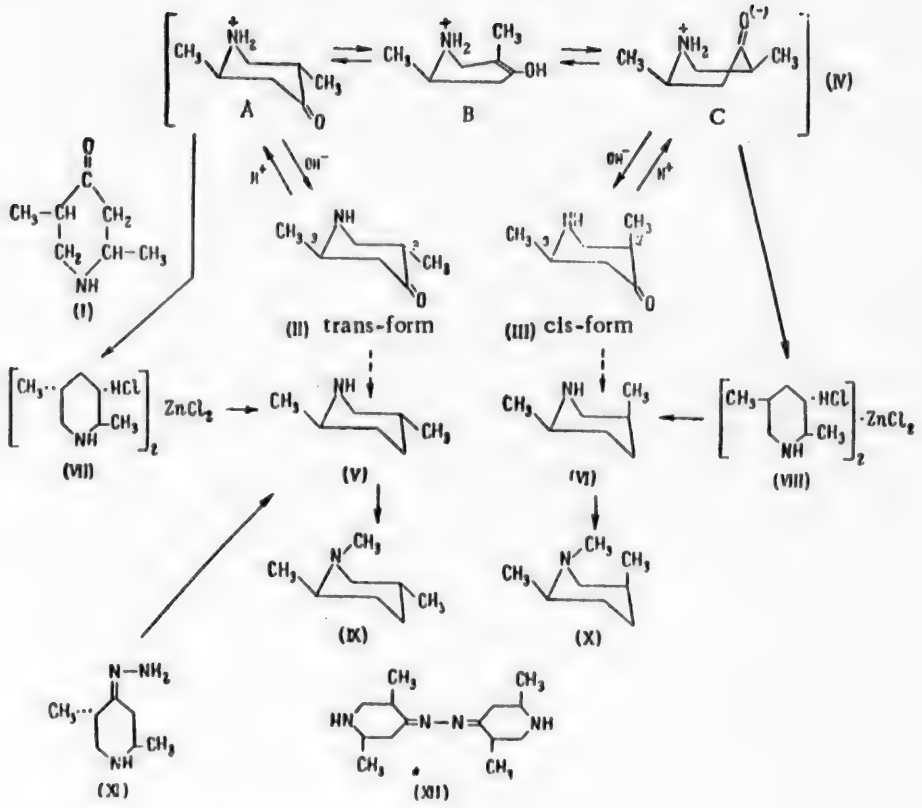
In a detailed study of methods for the reduction of 2,5-dimethyl-4-piperidone (I), having two asymmetric carbon atoms, we were able to isolate [1] three of the corresponding racemic piperidol derivatives of the four theoretically possible, and in this way show that the indicated piperidone (I) is capable of existing as two trans- and cis-isomers (II) and (III). However, all atempts to isolate them or to characterize them through crystalline derivatives (hydrochlorides, picrates) proved unsuccessful, apparently because of the case of their isomerization through the enol form.

In recent years, as is known [2], one of the homologs of piperidone (I) with the same number of asymmetric carbon atoms has found use in the synthesis of analgesics (promedol and its isomers), and because of this a study of the isomerism of this ketone became of interest not only from the scientific, but also from the practical standpoint [3].

In this paper an attempt was made to prove the existence of the trans- and cis-isomers (II) and (III) of piperidone (I) as the end hydrogenation products—the trans- and cis-isomers of 2,5-dimethylpiperidine (V) and (VI). Here the reduction of piperidone (I) by the Kizhner-Clemmensen procedure was selected as the method of eliminating the carbonyl oxygen. The heating of piperidone (I) with hydrazine hydrate gave hydrazone (XI) with m.p. 74°, corresponding to the trans-form of the piperidone (II), and a substantial amount of azine (XII). The reductive decomposition of hydrazone (XI) by the Kizhner technique led, as was to be expected, to the formation of the trans-isomer of 2,5-dimethylpiperidine (V). The second isomer of 2,5-dimethylpiperidine (VI) (cis-form) was obtained by the reduction of (IV) hydrochloride with amalgamated zinc dust. This isomer was isolated from the reduction products as the readily crystallizing double salt (VIII) with m.p. 159°, representing a compound with two molecules of piperidine (VI) hydrochloride and one molecule of zinc chloride. The isolation of piperidine (VI) from salt (VIII) was easily accomplished by decomposing the latter with aqueous NaOH solution. The physicochemical constants of the isomeric piperidines (V) and (VI) and of their crystalline derivatives are given in the table.

The high values of the refractive index, specific gravity, and boiling point of cis-piperidine (VI) are found to be in agreement with the von Auwers-Skita rule [4] in the interprepation of the conformational analysis theory [5].

Reduction of piperidone (I) hydrochloride with granulated (unamalgamated) zinc in hydrochloric acid enabled us to isolate a second double salt (VII) with m.p. 123°, from which we obtained the above described trans-form of piperidine (V) on treatment with sodium hydroxide. However, due to the difficulty with which salt (VII) crystallized, the thus-obtained piperidine (V) had somewhat high constants, apparently because of the presence of a small amount of cis-piperidine (VI) as impurity.



Properties of trans- and cis-Isomers of 2,5-Dimethylpiperidine

Isomers	Boiling point (pressure in mm)	$n^{20}D$	d^{20}_4	Melting point	
				phenyl-urethan	hydro-chloride
trans-Form (V) . . .	131—132°(736)	1.4430	0.8308	78—80°	197—198°
cis-Form (VI)	143.5—144 (729)	1.4667	0.8707	117—119	133—134

The fact that the two isomeric piperidines (V) and (VI) were obtained from the same starting piperidone (I) hydrochloride is evidence that this hydrochloride apparently exists in aqueous solution as two conformations A and C, isomerizing into each other through the enol form B and found in a state of equilibrium [6]. Both cations A and C correspond to the structure of two isomeric piperidones, respectively (II) and (III), in which connection the latter can arise from cation C when the hydrochloride is decomposed by alkali, by a turning of the two C-C bonds due to steric repulsion. Amalgamated zinc dust probably favors a greater reduction of cation C in the bathtub shape, while conversely, granulated zinc favors a greater reduction of cation A in the armchair shape, as a result of which cis-piperidine (VI) is formed predominantly in the first case, and trans-piperidine (V) in the second case. Both piperidines (V) and (VI) are easily methylated with a mixture of formalin and formic acid, and give the corresponding trans- and cis-1,2,5-trimethylpiperidines (IX) and (X).

Despite the fact that each of the obtained isomeric piperidines (V) and (VI) forms its own series of derivatives as described above, their individuality, taking into consideration the specific conditions of obtaining them, still requires confirmation synthetically.

EXPERIMENTAL

The 2,5-dimethyl-4-piperidone (I) used in our work was obtained as described earlier [7], and had the following constants: b.p. 78° (7 mm), $n^{20}D$ 1.4660; hydrochloride, m.p. 142-143° (from chloroform).

2,5-Dimethyl-4-piperidone hydrazone (XI). A mixture of 30 g of (I) and 25 g of 85% hydrazine hydrate was kept for 3 hr at room temperature and then it was heated on the boiling water bath for 30 min. The excess hydrazine hydrate and water were vacuum distilled, and the residue was fractionated in vacuo. We obtained 11.1 g of hydrazone (XI) with b.p. 100-101° at 1 mm, which completely solidified to crystals with m.p. 73-74°.

Found %: N 29.49, 29.83. $C_7H_{15}N_3$. Calculated %: N 29.76.

Most of the reaction product (14 g) remaining as a residue from the distillation of hydrazone (XI) was azine (XII) with b.p. 150-151° at 1.5 mm and m.p. 144-145° (from benzene).

Found %: N 21.25, 21.52. $C_{14}H_{26}N_4$. Calculated %: N 22.33.

Preparation of trans-2,5-dimethylpiperidine (V). A mixture of 9 g of hydrazone (XI) with m.p. 73-74° and 10 g of KOH, crushed into small pieces, was charged into a Claisen flask fitted with a Liebig condenser. The flask was immersed in a Wood's metal bath heated to 180°. A vigorous evolution of nitrogen began within 5 min and the reduction product began to distill at the same time. The decomposition of the hydrazone was complete in 7 min. The distilled product in ether solution was dried over solid NaOH. We obtained 5 g of (V).

B.p. 131-132° at 736 mm, $n^{20}D$ 1.4430, d^{20}_4 0.8308, MR_D 36.12; calc. 35.93.

Found %: C 74.21, 74.17; H 13.40, 13.43; N 12.43, 12.30. $C_7H_{15}N$. Calculated %: C 74.26; H 13.36; N 12.37.

The phenylurethan was obtained by mixing equivalent amounts of phenyl isocyanate and free base (V). Crystals with m.p. 78-80° (by precipitation from hot benzene solution with ligroine).

Found %: N 11.97, 12.00. $C_{14}H_{20}ON_2$. Calculated %: N 12.06.

The hydrochloride was obtained as a crystalline powder with m.p. 197-198° (from acetone).

Found %: N 9.40, 9.50. $C_7H_{16}NCl$. Calculated %: N 9.36.

Reduction of 2,5-dimethyl-4-piperidone (I) hydrochloride with amalgamated zinc in hydrochloric acid. To the amalgamated zinc, prepared from 150 g of zinc dust and 10 g of mercuric chloride [8], was added 75 ml of water, then 38 g of (IV) hydrochloride (m.p. 142-143°) was sifted in, and after this 100 ml of concd. hydrochloric acid was added. The vigorous reduction that started immediately then continued when the flask was heated under reflux in a Wood's metal bath at 100-110° for 14 hr, until nearly all of the zinc had dissolved. During this time 250 ml of concd. hydrochloric acid was added in 50-ml portions at equally spaced intervals. The solution after cooling was filtered and placed in a cold place (- 10 to - 15°). After 2 weeks the obtained crystals were suction-filtered on a glass filter, and then recrystallized 4 times from anhydrous alcohol. We obtained 16.2 g of double salt (VIII) with m.p. 157.5-159°, representing a compound containing 1 molecule of zinc chloride and 2 molecules of cis-piperidine (VI) hydrochloride.

Found %: N 6.34, 6.52. $C_{14}H_{32}N_2Cl_4Zn$. Calculated %: N 6.43.

cis-2,5-Dimethylpiperidine (VI). Fifteen grams of double salt (VIII) with m.p. 157.5-159° was dissolved by gentle heating in a small amount of water and then decomposed with aqueous sodium hydroxide solution. The free base was extracted with ether, dried over solid sodium hydroxide, and after removing the solvent was distilled. We obtained 5.5 g of (VI).

B.p. 143.5-144° at 729 mm; $n^{20}D$ 1.4667, d^{20}_4 0.8707, MR_D 36.05; calc. 35.93.

Found %: C 74.19, 74.15; H 13.40, 13.45; N 12.48, 12.25. $C_7H_{15}N$. Calculated %: C 74.26; H 13.36; N 12.37.

The phenylurethan was obtained as crystals with m.p. 117-119° (by precipitation from hot benzene solution with ligroine).

Found %: N 11.99, 12.05. $C_{14}H_{20}ON_2$. Calculated %: N 12.06.

The hydrochloride was obtained as a fine crystalline powder with m.p. 133-134° (by precipitation from alcohol solution with ether).

Found %: N 9.30, 9.42. $C_7H_{16}NCl$. Calculated %: N 9.36.

Reduction of 2,5-dimethyl-4-piperidone (I) hydrochloride with granulated zinc in hydrochloric acid. Into a round-bottomed flask fitted with a reflux condenser was placed a charge of 120 g of granulated zinc, 75 ml of water, 40 g of (IV) hydrochloride with m.p. 142-143°, obtained from piperidone (I), and 100 ml of concd. hydrochloric acid. The reduction was continued until all of the zinc had dissolved. During the course of reaction an additional 200 ml of concd. hydrochloric acid was added in 50-ml portions at equally spaced intervals. The clear solution was evaporated to $^1/_3$ volume using a water-jet pump. The long needles that deposited when the solution was allowed to stand in the cold for 2 days were filtered on a glass filter, and then were recrystallized three times by the technique of dissolving in alcohol and precipitating with ether. We obtained 7.2 g of double salt (VII) with m.p. 122-123°.

Found %: N 6.60, 6.63. $C_{14}H_{32}N_2Cl_4Zn$. Calculated %: N 6.43.

Decomposition of double salt (VII). Seven grams of salt (VII) with m.p. 122-123° was treated with 50 ml of 30% sodium hydroxide solution. The free base was extracted with ether, the ether solution dried over solid NaOH pellets, and after removal of the solvent the residue was distilled at atmospheric pressure. We obtained 3.0 g of trans-2,5-dimethylpiperidine:

B.p. 135.5-136.5° at 751 mm, $n^{20}D$ 1.4450, d^{20}_4 0.8345, MR_D 36.2; calc. 35.93.

This piperidine (V), containing some piperidine (VI) as impurity, forms a hydrochloride with m.p. 194-195°, which did not depress the melting point when mixed with the piperidine (V) hydrochloride obtained above by the Kizhner method ($n^{20}D$ 1.4430). The mother liquor from the separation of the salt (VII) crystals was treated with concd. sodium hydroxide solution and an additional 6.7 g of impure piperidine (V) ($n^{20}D$ 1.4445) and 6 g of starting piperidone (I) were isolated from the alkaline solution.

trans-1,2,5-Trimethylpiperidine (IX). A mixture of 2 g of trans-2,5-dimethylpiperidine (V) ($n^{20}D$ 1.4430), 1.6 g of 33% formalin, and 0.96 g of 85% formic acid was placed in a small flask fitted with a reflux condenser. The mixture warmed up, but the evolution of carbon dioxide began only when the mixture was heated on the boiling water bath, being ended in 1 hr. The flask contents were cooled and then made alkaline with NaOH solution. The free base was extracted with ether, the ether solution dried over solid NaOH, and after removal of the solvent the product was distilled twice at atmospheric pressure. We obtained 1.3 g of (IX).

B.p. 143-144° at 736 mm, $n^{20}D$ 1.4405, d^{20}_4 0.8208, MR_D 40.94; calc. 40.88.

Found %: N 11.21, 11.19. $C_8H_{17}N$. Calculated %: N 11.01.

The hydrochloride was obtained as crystals with m.p. 221-222° (by precipitation from alcohol solution with ether).

The picrate deposits immediately when methanol solutions of picric acid and free base are mixed; obtained as a fine powder with m.p. 176-177° (from methanol).

cis-1,2,5-Trimethylpiperidine (X). A mixture of 1.6 g of formalin and 0.96 g of formic acid was added to 2 g of cis-piperidine (VI) ($n^{20}D$ 1.4667). The mixture warmed up and the evolution of carbon dioxide bubbles began immediately, and ended in 20 min when the mixture was heated on the boiling water bath. The yellow solution was cooled and then worked up as described above. We obtained 1.4 g of (X).

B.p. 151-152° at 736 mm, $n^{20}D$ 1.4590, d^{20}_4 0.8570, MR_D 40.61; calc. 40.88.

Found %: N 11.15, 11.25. $C_8H_{17}N$. Calculated %: N 11.01.

Product (X) darkens quite rapidly on storage, but its physicochemical constants do not change on repeated distillation.

The hydrochloride was obtained as crystals with m.p. 153-154° (from alcohol solution by precipitation with ether).

The picrate was obtained as slender rods with m.p. 131-132° (from methanol).

SUMMARY

A study was made of the elimination of the carbonyl oxygen in 2,5-dimethyl-4-piperidone and its hydrochloride, and the two possible trans- and cis-2,5-dimethylpiperidines were obtained. Reduction of the piperidone by the Kizhner method gave the trans-piperidine, while the reduction of the hydrochloride of the same piperidone with amalgamated zinc dust gave the cis-piperidine as a crystalline compound with zinc chloride. Reduction of the same hydrochloride with granulated zinc in hydrochloric acid led to obtaining the trans-piperidine as another crystalline compound with zinc chloride. The formation of two isomeric piperidines from the same piperidone hydrochloride is explained in the light of the studies made by us.

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STEREOCHEMISTRY OF NITROGEN HETEROCYCLES

VIII. BENZOIC ESTERS OF ISOMERS OF 2-METHYL-4-HYDROXYDECAHYDROQUINOLINE AND 1,2-DIMETHYL-4-HYDROXYDECAHYDROQUINOLINE. NEW ANESTHETIC COMPOUNDS

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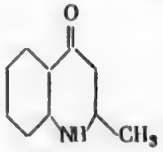
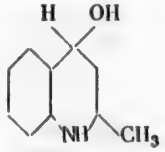
Original article submitted March 19, 1959

The development of new methods for obtaining various γ-piperidones [1] has made it possible to expand broadly the synthesis of medicinals of the piperidine series and at the same time give serious attention to stereochemistry problems, which have great importance for elucidating the relationship that exists between the physiological activity of compounds and not only their structure, but also their spatial structure. In this connection we are making a study of the stereoisomerism of various γ-piperidones and of the piperidine alcohols corresponding to them, and from these compounds we are synthesizing various stereoisomeric medicinals [2-4].



(I)



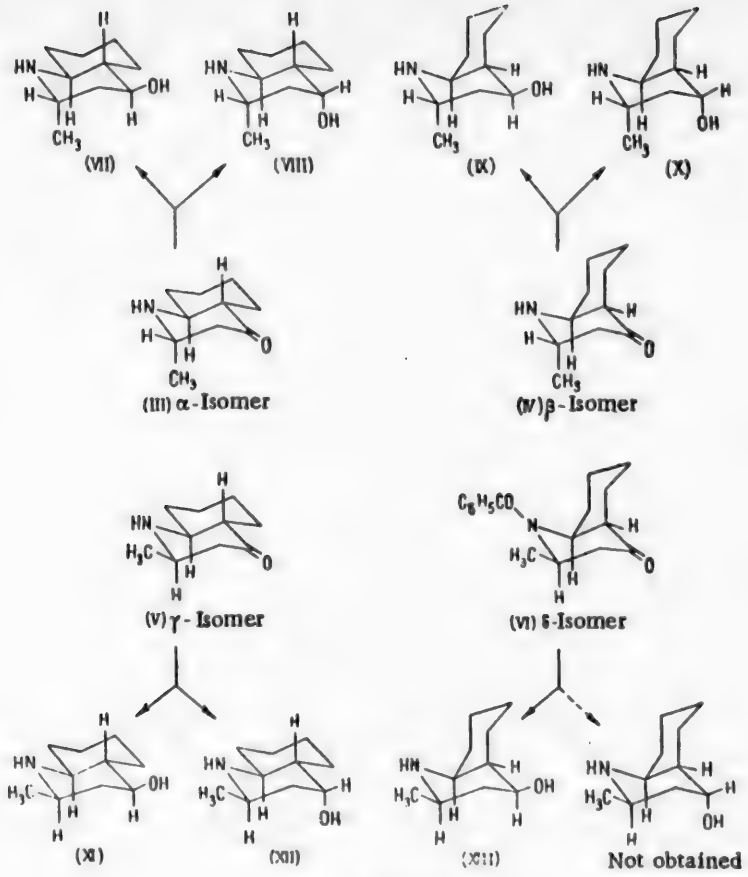
(II)

In our most recent work we studied the stereoisomerism of 2-methyl-4-ketodecahydroaquinoline (I) and also the stereoisomerism of the 2-methyl-4-hydroxydecahydroquinoline (II) corresponding to it. The rigid coupling of the rings in bicyclic piperidone (I) made it possible to separate the compound into its isomers and thus obtain all four of the racemic ketones (III), (IV), (V) and (VI) predicted by theory, and make a study of their properties and mutual transformations through the hydrochlorides [5].

A study of the reduction of the stereoisomeric ketones, and also of their derivatives, in turn made it possible to obtain seven of the eight theoretically possible racemic alcohol isomers of hydroxydecahydroquinoline (II), the structure of which, in accordance with the structure of the starting ketones, was depicted by us by the following spatial structures: (VII), (VIII), (IX), (X), (XI), (XII) and (XIII) [6, 7] (Scheme 1).

Secondary monocyclic γ-piperidine alcohols as the esters (eucaine, euphthalmine) recommended themselves even as early as the end of the 19th century as very effective synthetic analogs of the natural alkaloids (cocaine, atropine, etc.),and at the time found use in medicine as anesthetics and mydriatics. The high physiological activity of these compounds made them the subject of numerous and exhaustive investigations, in which connection the scientific and practical interest in their study has not decreased in importance even up to now [8].

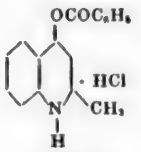
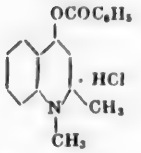
The ability to obtain the above described secondary bicyclic alcohols in large number creates favorable conditions for the synthesis of stereoisomeric anesthetics of the decahydroquinoline series, which have received little pharmacological attention up to the present. Scientific interest in such investigations is further enhanced by the fact that they permit studying the relationship between the pharmacological properties (anesthesia, toxicity,

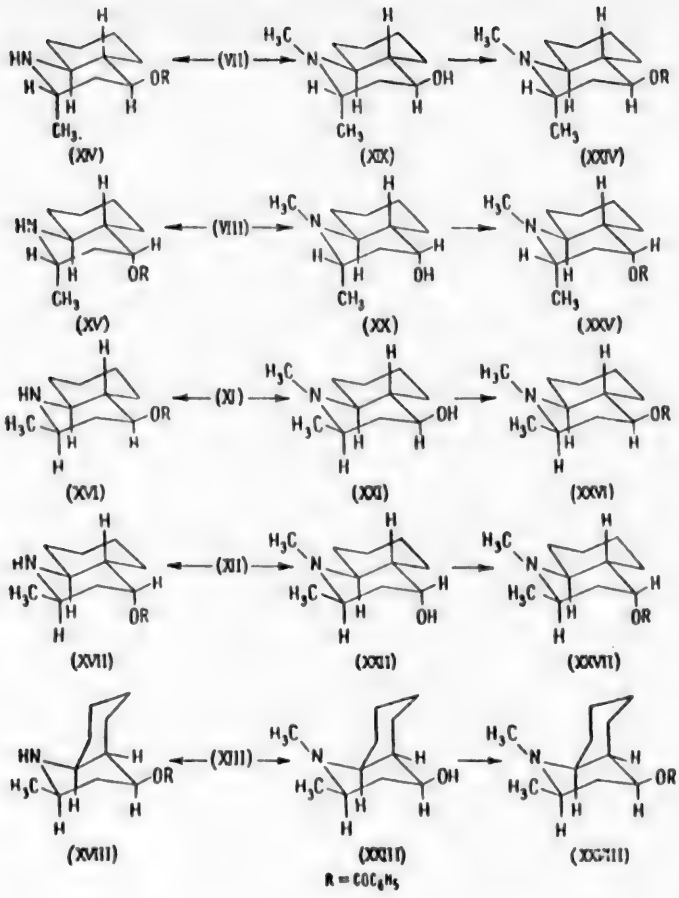


Scheme 1

TABLE 1

Anesthetic Action of Benzoates of Isomers of 2-Methyl-4-hydroxydecahydroquinoline and 1,2-Dimethyl-4-hydroxydecahydroquinoline

Formulas of the benzoates	No. of benzoate isomers	Anesthesia in Regnier units (average values) concentration in (%)				Toxicity (in mg/g of animal weight)	
		0.25	0.5	1.0	2.0	minimum lethal dose	absolute lethal dose
	(XIV)	441	1103	Insoluble		0.2	0.4
	(XV)	484	1129	The same		0.05	0.2
	(XVI)	422	710	"	"	0.3	0.4
	(XVII)	456	993	990	1253	0.2	0.4
	(XVIII)	322	921	Insoluble		0.4	—
	(XXIV)	798	1216	1241	1298	0.1	0.3
	(XXV)	943	1212	1240	1258	0.15	0.2
	(XXVI)	946	1128	1245	1211	0.5	1.0
	(XXVII)	786	1018	1078	1200	0.2	0.35
	(XXVIII)	526	745	914	836	0.3	0.7
Novocaine	—	109	181	255	309	0.3	0.6
Cocaine	—	158	401	573	730	0.05—0.07	0.15—0.7
Dicaine	—	1182	1194	1289	1300	0.05	—



Scheme 2

etc.) of compounds and a whole series of factors: the character of the linking (cis- or trans-) of the piperidine and cyclohexane rings, steric alignment of the hydroxyl group, and other characteristics of the spatial structure of the investigated alcohols.

In this paper we describe the synthesis of the benzoates of five of the more readily available alcohols, four of which have a trans-linking of the rings (VII, m.p. 134°; VIII, m.p. 128°; XI, m.p. 144°; XII, m.p. 158°), and the fifth (XIII, m.p. 115°) with a cis-linking of the rings, and we also describe the synthesis of the benzoates of the N-methyl derivatives of these same alcohols (Scheme 2).

The benzoates of 2-methyl-4-hydroxydecahydroquinoline (XIV), (XV), (XVI) and (XVII) were obtained in good yield by heating the hydrochlorides of the racemic alcohols (VII), (VIII), (XI) and (XII) with benzoyl chloride. Benzoate (XVIII) was obtained from the N-benzoyl derivative of alcohol (XIII) by the earlier described method [7]. The heating of these same alcohols with a mixture of formalin and formic acid enabled us to obtain the five corresponding racemates of 1,2-dimethyl-4-hydroxydecahydroquinoline (XIX, m.p. 117°; XX, m.p. 149°; XXI, m.p. 88°; XXII, m.p. 131°; XXIII, m.p. 100°) in better than 90% yield, which in turn were converted to the corresponding benzoates (XXIV), (XXV), (XXVI), (XXVII), and (XXVIII).

All of the obtained benzoates as the hydrochlorides were tested pharmacologically• for anesthetic properties and toxicity. The test results are given in Table 1, and from this data it can be seen that most of

•The pharmacological testing was done in the Department of Pharmacology of the Alma-Ata Medical Institute and in the Pharmacology Laboratory of the Institute of Physiology of the Academy of Sciences of the Kazakh. SSR under the general direction of I. I. Sivertsev.

TABLE 2

Properties of Isomers of 1,2-Dimethyl-4-hydroxydecahydroquinoline and Their Derivatives

Formulas of isomers (a), their hydrochlorides (b), and picrates (c)		Time of methylation (in min)	Yield (in %)	Melting point	% N		% C		% H		Recrystallization solvent
					found	calculated	found	calculated	found	calculated	
(XIX)	a) $C_{11}H_{21}ON$	30	93.5	116—117°	7.83, 7.67	7.64	72.90, 72.77	72.07	11.91, 11.73	11.54	Acetone
	b) $C_{11}H_{22}ONCl$	—	—	238—239	5.91, 5.72	6.37	—	—	—	—	Anhydrous alcohol
	c) $C_{17}H_{24}O_8N_4$	—	—	149—149.5	13.24, 13.02	13.59	—	—	—	—	The same
(XX)	a) $C_{11}H_{21}ON$	20	92.5	148—149	7.78, 7.76	7.64	72.91, 72.65	72.07	11.38, 11.56	11.54	Acetone
	b) $C_{11}H_{22}ONCl$	—	—	257—258	6.21, 6.49	6.37	—	—	—	—	Anhydrous alcohol
	c) $C_{17}H_{24}O_8N_4$	—	—	175—176	13.60, 13.74	13.59	49.94, 49.95	49.51	6.01, 5.95	5.86	The same
(XXI)	a) $C_{11}H_{21}ON$	45	90.2	87—88	7.75, 7.79	7.64	72.99, 72.82	72.07	11.79, 11.80	11.54	Petroleum ether (40-50°)
	b) $C_{11}H_{22}ONCl$	—	—	173—175	5.55, 5.71	6.36	—	—	—	—	Anhydrous alcohol
	c) $C_{17}H_{24}O_8N_4$	—	—	140—142	13.68, 13.88	13.59	—	—	—	—	The same
(XXII)	a) $C_{11}H_{21}ON$	25	79.2	130—131	7.68, 7.86	7.64	—	—	—	—	Acetone
	b) $C_{11}H_{22}ONCl$	—	—	150—151	6.08, 6.15	6.36	—	—	—	—	Anhydrous alcohol
	c) $C_{17}H_{24}O_8N_4$	—	—	192—193	13.62, 13.82	13.59	—	—	—	—	Alcohol
(XXIII)	a) $C_{11}H_{21}ON$	25	80.0	99—100	7.78, 7.89	7.64	71.65, 71.52	72.07	11.53, 11.51	11.54	Petroleum ether (50-60°)
	b) $C_{11}H_{22}ONCl$	—	—	192—194	—	—	—	—	—	—	Anhydrous alcohol and ether
	c) $C_{17}H_{24}O_8N_4$	—	—	149—151	13.31, 13.50	13.59	49.55, 49.56	49.51	5.94, 5.85	5.86	Alcohol

TABLE 3

Properties of Benzoates of 2-Methyl-4-hydroxydecahydroquinoline and Their Derivatives

Formulas of benzoates (a), their hydrochlorides (b), and picrates (c)		Benzoylation temperature	Yield (in %)	Melting point	% N		% C		% H		Recrystallization solvent
					found	calculated	found	calculated	found	calculated	
(XIV)	a) $C_{17}H_{23}O_2N$ *	183—190°	84.6		5.31, 5.45	5.13	74.49, 74.27	74.66	8.63, 8.57	8.48	
	b) $C_{17}H_{24}O_2NCl$	—	—	283—284°	4.32, 4.24	4.52	—	—	—	—	Anhydrous alcohol
	c) $C_{23}H_{26}O_9N_4$	—	—	208—209	11.27, 11.21	11.15	55.38, 55.23	54.97	5.33, 5.25	5.21	Alcohol
(XV)	a) $C_{17}H_{23}O_2N$	197—198	64.0	77—78	5.09, 5.00	5.13	—	—	—	—	Petroleum ether (40-50°)
	b) $C_{17}H_{24}O_2NCl$	—	—	269—271	4.49, 4.63	4.52	—	—	—	—	Anhydrous alcohol
	c) $C_{23}H_{26}O_9N_4$	—	—	256—257	13.24, 13.05	11.85	—	—	—	—	The same
(XVI)	a) $C_{17}H_{23}O_2N$	190—193	53.6	87— 87.5	5.40, 5.42	5.13	—	—	—	—	Petroleum ether (50-60°)
	b) $C_{17}H_{24}O_2NCl$	—	—	270—272	4.53, 4.39	4.52	—	—	—	—	Anhydrous alcohol
	c) $C_{23}H_{26}O_9N_4$	—	—	240—241	—	—	—	—	—	—	The same
(XVII)	a) $C_{17}H_{23}O_2N$ **	197—199	83.5		5.79, 5.59	5.13	75.10, 75.17	74.66	8.47, 8.66	8.48	
	b) $C_{17}H_{24}O_2NCl$	—	—	214—215	4.35, 4.45	4.52	—	—	—	—	Anhydrous alcohol
	c) $C_{23}H_{26}O_9N_4$	—	—	271—273	11.32, 11.12	11.15	54.72, 54.33	54.97	5.37, 5.06	5.21	Acetone
(XVIII)	a) $C_{17}H_{23}O_2N$ [7]	135—140	50.2	75—76	5.57, 5.72	5.13	74.68, 74.46	74.66	8.59, 8.39	8.48	Petroleum ether (50-60°)
	b) $C_{17}H_{24}O_2NCl$	—	—	304—305	4.87, 4.67	4.52					Alcohol
	c) $C_{23}H_{26}O_9N_4$	—	—	216—217	11.23, 10.92	11.15	54.88, 54.70	54.97	5.31, 5.83	5.21	Alcohol

* d^{20}_4 1.0869, $n^{20}D$ 1.5396, MR_D 78.76; calc. 77.96; b.p. 170-171° at 2 mm.

** d^{20}_4 1.0874; $n^{20}D$ 1.5380, MR_D 78.63; calc. 77.96; b.p. 166-167° at 3 mm.

TABLE 4

Properties of Benzoates of 1,2-Dimethyl-4-hydroxydecahydroquinoline and Their Derivatives

Formulas of benzoates (a), their hydrochlorides (b), and picrates (c)		Benzoylation temperature	Yield (in %)	Melting point	% N		% C		% H		Recrystallization solvent
					found	calculated	found	calculated	found	calculated	
(XXIV)	a) $C_{18}H_{25}O_2N$	160—165°	99.0	62—63°	4.98, 4.87	4.87	—	—	—	—	Acetone
	b) $C_{18}H_{26}O_2NCl$	—	—	269—270	4.17, 4.35	4.33	—	—	—	—	Anhydrous alcohol
	c) $C_{24}H_{28}O_9N_4$	—	—	—	—	—	—	—	—	—	
(XXV)	a) $C_{18}H_{25}O_2N$ *	160—165	84.0	41—42	4.64, 4.52	4.87	—	—	—	—	
	b) $C_{18}H_{26}O_2NCl$	—	—	204—205	4.45, 4.34	4.33	—	—	—	—	Anhydrous alcohol
	c) $C_{24}H_{28}O_9N_4$	—	—	233—234	10.86, 11.30	10.85	—	—	—	—	Alcohol
(XXVI)	a) $C_{18}H_{25}O_2N$ **	145—150	97.0		4.56, 4.57	4.87	75.53, 75.83	75.22	9.31, 9.27	8.76	
	b) $C_{18}H_{26}O_2NCl$	—	—	217—218	4.54, 4.43	4.33	—	—	—	—	Alcohol with ether
	c) $C_{24}H_{28}O_9N_4$	—	—	192—193	11.46, 11.71	10.85	—	—	—	—	Alcohol
(XXVII)	a) $C_{18}H_{25}O_2N$ ***	140—145	87.7		5.26, 5.38	4.87	75.50, 75.72	75.22	8.99, 9.18	8.76	
	b) $C_{18}H_{26}O_2NCl$	—	—	Hygroscopic	4.21, 4.06	4.33	—	—	—	—	Anhydrous alcohol with ether
	c) $C_{24}H_{28}O_9N_4$	—	—	212—213	10.38, 10.36	10.85	—	—	—	—	Acetone
(XXVIII)	a) $C_{18}H_{25}O_2N$	150—155	95.0	57—58	4.70, 4.81	4.87	—	—	—	—	Petroleum ether (b. p. up to 50°)
	b) $C_{18}H_{26}O_2NCl$	—	—	232—234	4.17, 4.34	4.33	—	—	—	—	Alcohol

*d^{20}_4 1.0844, $n^{20}D$ 1.5417, MR_D 83.2; calc. 82.92; b.p. 148-149° at 1 mm.
**d^{20}_4 1.0702, $n^{20}D$ 1.5380, MR_D 83.87; calc. 82.92; b.p. 165-167° at 1 mm.
***d^{20}_4 1.0723, $n^{20}D$ 1.5368, MR_D 83.85; calc. 82.92; b.p. 165-168° at 2 mm.

the synthesized compounds show a high anesthetic action, surpassing by many times the anesthetic action of novocaine and being substantially more powerful than cocaine, especially at low concentrations, while some of them even approach the very powerful anesthetic dicaine in this respect, at the same time possessing a substantially lower toxicity. From the data in Table 1 it can also be seen that the N-methyl derivatives of the benzoates (XXIV-XXVIII) show a higher anesthetic action than do the corresponding benzoates (XIV-XVIII) with a secondary amino group. As yet it is still difficult to make any general conclusions as to the rules governing the relationship between the pharmacological activity of the synthesized compounds and their spatial structure, since for this it is also necessary to investigate the other alcohols (IX and X); however even at the present time it can be stated that synthesizing anesthetics with a decahydroquinoline nucleus from the above described stereoisomeric alcohols appears highly promising.

EXPERIMENTAL

The starting racemates of 2-methyl-4-hydroxydecahydroquinoline (VII, m.p. 133-134°; hydrochloride, m.p 270-271°; VIII, m.p. 127-128°; hydrochloride, m.p. 197-198°; XI, m.p. 143-144°; hydrochloride, m.p. 310-312°; XII, m.p. 157-158°; hydrochloride, 247-248°; XIII, m.p. 114-115°; hydrochloride, m.p. 278-279°), used in the present study, were synthesized as described earlier [6, 7].

The isomers of 1,2-dimethyl-4-hydroxydecahydroquinoline[(XIX), (XX), (XXI), (XXII) and (XXIII)] used to synthesize the benzoates, were obtained by heating the corresponding racemates of 2-methyl-4-hydroxydecahydroquinoline[(VII), (VIII), (XI), (XII) and (XIII)]with formalin and formic acid under reflux on the boiling water bath. The formalin and 90% formic acid were taken in 5 to 20% excess. The reaction mixture was heated under reflux until the evolution of carbon dioxide ceased completely. After cooling, the methylation products, in most cases obtained in the crystalline state, were treated with potassium carbonate, dried in ether solution, and after removal of the solvent were recrystallized to a constant melting point (1 to 2 recrystallizations). The hydrochlorides of the methylated alcohols were obtained by neutralizing the free bases in anhydrous alcohol solution with dry hydrogen chloride. The picrates were obtained by mixing separately prepared alcohol solutions of equivalent amounts of free base and picric acid. The constants of the 5 synthesized isomers of 1,2-dimethyl-4-hydroxydecahydroquinoline, their hydrochlorides, and their picrates, are all given in Table 2.

The benzoates were synthesized by heating the hydrochlorides of the stereoisomers of 2-methyl-4-hydroxydecahydroquinoline and 1,2-dimethyl-4-hydroxydecahydroquinoline with excess benzoyl chloride (about 1.5 moles) under reflux in a Wood's metal bath. The temperature was raised at a rate of approximately 10° per minute until hydrogen chloride began to evolve, and then the reaction mixture was kept at this temperature until the evolution of hydrogen chloride had ceased completely. The reaction product, obtained as a glassy mass, was dissolved in water in the presence of ether. The aqueous solution of the hydrochloride was separated, repeatedly washed with ether to remove excess benzoyl chloride, and then was treated with potassium carbonate; the free base of the benzoate was extracted with ether, dried over sodium sulfate, and after removal of the ether was vacuum distilled. In the case of benzoates (XIV-XVII) and (XIX) the treatment of the reaction products with water and ether resulted in the separation of the crystalline hydrochlorides, which were filtered, washed with ether, and recrystallized from anhydrous alcohol. The water-soluble portion of the hydrochloride was decomposed with potassium carbonate, as described above, and the thus obtained additional amounts of benzoates were again converted to the hydrochlorides. The purified hydrochlorides were then converted in customary manner to the corresponding free bases for the purpose of characterizing them chemically. Nine benzoates were synthesized in this manner. Of them, 4 benzoates of 2-methyl-4-hydroxydecahydroquinoline (XIV-XVII), summarized in Table 3, were obtained from the corresponding hydrochlorides of alcohols (VII), (VIII), (XI) and (XII). The 5th benzoate of this series (XVIII) was synthesized from the N-benzoyl derivative of alcohol (XIII), as described earlier [7]. The benzoates of 1,2-dimethyl-4-hydroxydecahydroquinoline (XXIV-XXVIII) were obtained in a similar manner from the hydrochlorides of alcohols (XIX-XXIII), and are described in Table 4. The hydrochlorides and picrates of all the benzoates were prepared as described above.

SUMMARY

The benzoates of five racemic isomers of 2-methyl-4-hydroxydecahydroquinoline were synthesized, as well as the benzoates of the five corresponding isomers of 1,2-dimethyl-4-hydroxydecahydroquinoline, and the results of their pharmacological testing as local anesthetics were reported.

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SYNTHESIS AND PROPERTIES OF α,ω-POLYCHLORODISILALKANES

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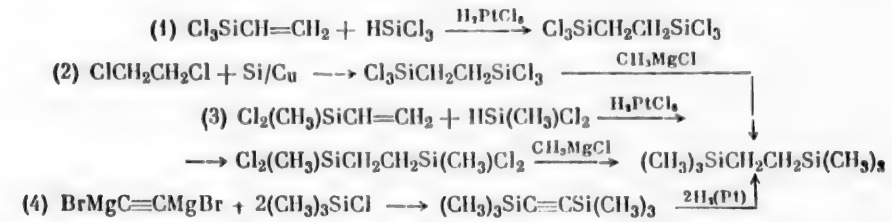
α,ω-Polychlorodisilanes are obtained by the direct method, i.e., by the reaction of dichloroalkanes [1], alkenes [2] or chloroalkylsilanes [3] with Si/Cu alloy at elevated temperatures. The synthesis of α,ω-polychlorodisilanes of type $\equiv SiCH_2CH_2Si\equiv$ or $\equiv SiCH_2CH_2CH_2Si\equiv$ can also be accomplished by the addition of silicon hydrides to vinyl- and allylsilane chlorides. This last reaction is usually run in sealed ampuls or autoclaves using various catalysts, for example, peroxides [4], platinized carbon [5], pyridine [6], and others. The second method of obtaining polychlorodisilanes differs favorably from the direct synthesis method by higher yields of the desired products and a simpler composition of the reaction products.• Recently [8] chloroplatinic acid was proposed as a catalyst for the addition of silicon hydrides to olefins, and here the bis(chloroalkylsilyl)ethanes are obtained at comparatively low temperatures and pressures [9]. Finally, in our previous paper [10] we reported on the synthesis of α,ω-dichlorodisilanes in good yields by the addition of dialkylchlorosilanes to divinyl- and diallylsilicon-containing compounds, and also to 1,5-hexadiene, where the reaction was run at atmospheric pressure and a short heating of the reactants in the presence of H_2PtCl_6.

The purpose of the present investigation was: first, to establish the order of addition of silicon hydrides in the presence of H_2PtCl_6 to vinyl- and allyl-containing organosilicon compounds, and second, to use this extremely simple method to synthesize both known α,ω-polychlorodisilanes previously obtained by other methods, and new members of the α,ω-polychlorodisilanes with di-, tri- and hexamethylene, and also silicohydrocarbon and hydrocarbonsiloxane bridges.

The order of addition of the chloro(or chloroalkyl)silyl groups to vinyl-containing organosilicon compounds was proved in the following manner.


(1) Cl3SiCH=CH2 + HSiCl3 H2PtCl6 Cl3SiCH2CH2SiCl3
(2) ClCH2CH2Cl + Si/Cu → Cl3SiCH2CH2SiCl3 CH3MgCl
(3) Cl2(CH3)SiCH=CH2 + HSi(CH3)Cl2 H2PtCl6
→ Cl2(CH3)SiCH2CH2Si(CH3)Cl2 CH3MgCl (CH3)3SiCH2CH2Si(CH3)3
(4) BrMgC≡CMgBr + 2(CH3)3SiCl → (CH3)3SiC≡CSi(CH3)3 2H2(Pt)

The properties of the compound obtained according to Scheme (1) proved to be identical with the properties of the 1,2-bis(trichlorosilyl)ethane prepared by direct synthesis [1] according to Scheme (2). The Raman spectrum•• and other properties of the completely methylated adduct, obtained according to Scheme (3), proved

•At the present time this method also assumes interest for the reason that many vinyl- and allylchlorosilanes can be easily obtained, for example, by the method of [7].

••The Raman and infrared spectra given in this investigation were taken and interpreted by L. A. Leites and Yu. P. Egorov, for which the authors express their thanks.

Fig. 1. Infrared spectrum of trichlorosilane–1,5-hexadiene adduct (taken using an IRS-12 spectrograph and LiF prism).

to be identical with the spectrum and properties of the 1,2-bis(trimethylsilyl)ethane prepared from the hexachloride according to Scheme (2), and also obtained earlier [11, 6] according to Scheme (4). It proved that methyldichlorosilane adds to both allyltrichlorosilane and allyltrimethylsilane contrary to the Markovnikov rule. After methylation, both of these adducts had the same properties and the same Raman spectrum, completely identical with the spectrum of 1,3-bis(trimethylsilyl)propane, obtained earlier by a method that excluded the formation of the isomeric 1,2-bis (trimethylsilyl) propane.

The infrared spectrum (Fig. 1) of the adduct of two moles of trichlorosilane with 1 mole of 1,5-hexadiene showed in the region of the C-H valence vibrations only 2 maxima at 2937 and 2862 cm^{-1}, characterizing the $=CH_2$ group; the frequencies characteristic for the $-CH_3$ group were not observed. As a result, $Cl_3Si(CH_2)_6SiCl_3$ can be the only structure possible for this adduct.

It is interesting to mention that, in contrast to our results [Scheme (1)], Nozakura [6] observed the addition of silicochloroform to vinyltrichlorosilane according to the Markovnikov rule: Thereaction was run in the presence of complex catalysts, containing pyridine, as a result of which this investigator obtained both possible adducts: $Cl_3SiCH_2SiCl_3$ and $Cl_3SiCHSiCl_3$ (with CH_3 on the CH carbon).

All of the above discussed cases of the addition of the silyl group to vinyl- and allyl-containing compounds, and also to 1,5-hexadiene, enable us to postulate with a great deal of probability that the addition of the silyl group in the presence of H_2PtCl_6 goes contrary to the Markovnikov rule and in accordance with the general schemes (5-9).

(5) $\equiv SiCH{=}CH_2 + HSi\equiv \longrightarrow \equiv SiCH_2CH_2Si\equiv$

(6) $CH_2{=}CHCH_2Si(R)(R)CH_2CH{=}CH_2 + 2HSi\equiv \longrightarrow \equiv SiCH_2CH_2CH_2Si(R)(R)CH_2CH_2CH_2Si\equiv$

(7) $\equiv SiCH_2CH{=}CH_2 + HSi\equiv \longrightarrow \equiv SiCH_2CH_2CH_2Si\equiv$

(8) $CH_2{=}CHSi(R)(R)-O-Si(R)(R)CH{=}CH_2 + 2HSi\equiv \longrightarrow \equiv SiCH_2CH_2Si(R)(R)-O-Si(R)(R)CH_2CH_2Si\equiv$

(9) $CH_2{=}CHCH_2CH_2CH{=}CH_2 + 2HSi\equiv \longrightarrow \equiv SiCH_2CH_2CH_2CH_2CH_2CH_2Si\equiv$

According to reaction (5) the vinyl-containing compound can be: $Cl_3SiCH=CH_2$, $Cl_2RSiCH=CH_2$, $ClR_2SiCH=CH_2$, $R_3SiCH=CH_2$ ($R = CH_3, C_2H_5$), while the silicon hydride can be: Cl_3SiH, Cl_2RSiH, ClR_2SiH [10] and R_3SiH ($R = CH_3, C_2H_5, C_6H_5$); here the yield of the adduct remained high, independent of the character of the radicals linked to the silicon of either reaction component (see Table 1). In reactions (6), (8) and (9) the silicon hydride reacts in a stepwise manner. The properties of the obtained adducts and some of their derivatives are given in Table 2.

EXPERIMENTAL

The starting alkenyl-containing organosilicon compounds and silicon hydrides were prepared by known procedures and were purified by distillation through a column (20 theoretical plates).

TABLE 1

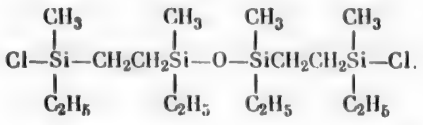
Expt. No.	Components		Time of heating (in hr)	Appearance of reaction mixture after heating	Final temperature of heating reaction mixture	Yield of adduct (in %)
	alkenyl-containing compound	silicon hydride				
1	$Cl_3SiCH=CH_2$	$HSiCl_3$	3.5	Light brown	178°	93
2	$Cl_2(CH_3)SiCH=CH_2$	$HSi(CH_3)Cl_2$	1.5	Light yellow	198	94
3	$Cl_2(CH_3)SiCH=CH_2$	$HSi(C_2H_5)Cl_2$	0.5	Colorless	192	92
4	$Cl_3SiCH=CH_2$	$HSi(C_6H_5)Cl_2$	1.5	The same	220	77
5	$(C_2H_5)_2(CH_3)SiCH=CH_2$	$HSi(CH_3)(C_2H_5)_2$	1.0	" "	150	79
6	$[(C_2H_5)(CH_3)(CH_2=CH)Si]_2O$	$HSi(CH_3)Cl_2$	1.0	Light yellow	230	91
7	$Cl_3SiCH_2CH=CH_2$	$HSi(CH_3)Cl_2$	3.5	Dark	196	90
8	$(CH_3)_3SiCH_2CH=CH_2$	$HSi(CH_3)Cl_2$	0.5	Colorless	146	95
9	$(C_2H_5)_2Si(CH_2CH=CH_2)_2$	$HSi(CH_3)Cl_2$	3.0	Yellow	180	79 *
10	$(CH_2=CHCH_2-)$	$HSiCl_3$	3.5	Colorless	185	68
11	$(CH_2=CHCH_2-)$	$HSi(CH_3)Cl_2$	1.0	The same	185	61 **
12	$(CH_2=CHCH_2-)$	$HSi(C_2H_5)Cl_2$	2.0	Light yellow	190	77

* Based on the broad fraction 138-149° at 2 mm.

** Besides $[Cl_2(CH_3)SiCH_2CH_2CH_2-]_2$, we also isolated the adduct of 1 mole of $HSi(CH_3)Cl_2$ and 1 mole of 1,5-hexadiene with b.p. 51° (3 mm), n^{20}_D 1.4530, d^{20}_4 1.0053.

1-Trichlorosilyl-3-methyldichlorosilylpropane (Table 2, No. 10). A charge of 17.5 g (0.1 mole) of allyltrichlorosilane and 2 drops of 0.1 N H_2PtCl_6 solution in isopropyl alcohol was placed in a flask fitted with a dropping funnel, thermometer, and efficient water condenser. After heating the flask contents to the boil, 3 ml of the weighed amount (11.5 g; 0.1 mole) of methyldichlorosilane was added to the mixture. After some time the temperature of the reaction mixture began to rise, and then the remainder of the methyldichlorosilane was added to the flask in small portions. The reaction mixture was heated for 3.5 hr. On reaching 196° the heating was stopped, and the reaction mixture was fractionally distilled in vacuo, b.p. 109-111° (18 mm), yield 28 g.

Experiments 1-12, the results of which are summarized in Table 1, were run in a similar manner; in Expts. 6, 9, 10-12 we took 2 moles of silicon hydride per mole of alkenyl-containing compound. In the other experiments the ratio of the reactants was equimolar. In the reaction between sym-divinyldiethyldimethyldisiloxane and methylethylchlorosilane the reactants were taken in a 1 : 1 mole ratio; here the silicon hydride reacted completely, and from the reaction mixture we isolated the adduct of 1 mole of silicon hydride with 1 mole of divinyldiethyldimethyldisiloxane (see No. 17 in Table 2), and



obtained earlier [10]. In some instances the reaction stopped during the addition of the hydride-containing compound (especially if added rapidly), in which case another drop of the catalyst was added to the reaction mixture; in the cases where the indicated reactions went with considerable heat evolution, the mixing of the reagents was done without applying heat to the reaction mixture, and here the temperature stayed at 90-110° because of the reaction heat.

The methylation of $Cl_2(CH_3)SiCH_2CH_2CH_2SiCl_3$ (25 g) was run in convential manner, using the methylmagnesium chloride prepared from 16.8 g of magnesium. Fractional distillation through a column (20 theoretical plates) gave 14.2 g (94%) of 1,3-bis(trimethylsilyl)propane (Table 2, No. 12). The distillation curve indicates the presence of only one compound (Fig. 2).

TABLE 2

Properties of α,ω-Polychlorodisilanes and Their Derivatives

Expt. No.	Adducts and their derivatives	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Empirical formula	Elemental analysis
1	$Cl_3SiCH_2CH_2SiCl_3$ 1,2-bis(Trichlorosilyl)ethane	200—201.5° (757) m.p. 25.2°	—	—	—	—	$C_2H_4Si_2Cl_6$	—
2	$Cl_3SiCH_2CH_2Si(C_6H_5)Cl_2$ 1-Trichlorosilyl-2-phenyldichlorosilylethane	118.5 (1.5)	1.3714	1.5310	76.1	76.4	$C_8H_9Si_2Cl_5$	Found %: Si 16.0, 16.4 Calculated %: Si 16.6
3	$Cl_2(CH_3)SiCH_2CH_2Si(CH_3)Cl_2$ 1,4-bis(Methyldichlorosilyl)ethane	109—111 (30) m.p. 32.5	—	—	—	—	$C_4H_{10}Si_2Cl_4$	Found %: Cl 55.4, 55.4 Calculated %: Cl 55.5
4	$Cl_2(CH_3)SiCH_2CH_2Si(C_2H_5)Cl_2$ • 1-(Methyldichlorosilyl)-2-(ethyldichlorosilyl)ethane	231—232 (758)	1.2233	1.4170	61.7	61.5	$C_5H_{12}Si_2Cl_4$	Found %: Si 21.1, 20.6; C 22.1, 22.4; H 4.5, 4.4; Cl 50.5, 51.1. Calculated %: Si 20.8; C 22.2; H 4.5; Cl 52.5.
5	$(C_2H_5)_2(CH_3)SiCH_2CH_2Si(CH_3)(C_2H_5)_2$ • 1,2-bis(Diethylmethylsilyl)ethane	105 (10)	0.8038	1.4475	76.5	76.5	$C_{12}H_{30}Si_2$	Found %: Si 23.7, 23.8; C 62.5, 62.7; H 12.9, 31.1. Calculated %: Si 24.3; C 62.5; H 13.2
6	$(CH_3)_3SiCH_2CH_2Si(CH_3)_3$ 1,2-bis(Trimethylsilyl)ethane	150.5—151.5 (762)	0.7522	1.4195	—	—	$C_8H_{12}Si_2$	
7	$(CH_3COO)_2(CH_3)SiCH_2CH_2Si(C_2H_5)(OOCCH_3)_2$ • 1-Methyldiacetoxysilyl-2-ethyldiacetoxysilylethane	167—169 (2) m.p. 34.5—35	—	—	—	—	$C_{13}H_{24}O_8Si_2$	Found %: Si 15.5, 15.8 Calculated: Si 15.4
8	$(C_2H_5O)_2(CH_3)SiCH_2CH_2Si(OC_2H_5)_2(CH_3)$ 1,2-bis(Methyldiethoxysilyl)ethane	79—80 (1.5)	0.9300	1.4180	79.9	80.0	$C_{12}H_{30}O_4Si_2$	Found %: Si 19.2, 19.4. Calculated %: Si 19.1.

• New Compounds.

TABLE 2 (Contd.)

Expt. No.	Adducts and their derivatives	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Empirical formula	Elemental analysis
9	$[Cl_2(CH_3)SiCH_2CH_2Si(CH_3)(C_2H_5)-]_2O$ • Symmetrical di-[(methyldichlorosilyl)ethyl]-dimethyl-diethyldisiloxane	137—138° (3)	1.0850	1.4650	113.2	112.8	$C_{12}H_{30}OSi_4Cl_4$	Found %: Si 24.8, 24.8; C 32.5, 32.7; H 7.1, 7.1; Cl 31.3, 31.7. Calculated %: Si 25.2; C 32.4; H 6.8; Cl 31.9
10	$Cl_2SiCH_2CH_2CH_2Si(CH_3)Cl_2$ 1-Trichlorosilyl-3-methyldichlorosilylpropane	110—110.5 (18)	1.3223	1.4711	61.3	61.2	$C_4H_9Si_2Cl_5$	Found %: Cl 61.1, 61.3. Calculated %: Cl 61.2
11	$(CH_3)_3SiCH_2CH_2CH_2Si(CH_3)Cl_2$ 1-Trimethylsilyl-3-methyldichlorosilylpropane	199—200 (742)	0.9653	1.4430	—	—	$C_7H_{18}Si_2Cl_2$	—
12	$(CH_3)_3SiCH_2CH_2CH_2Si(CH_3)_3$ 1,3-bis(Trimethylsilyl)propane	171.7 (747)	0.7561	1.4220	—	—	$C_9H_{24}Si_2$	—
13	$[Cl_2(CH_3)SiCH_2CH_2CH_2]_2Si(C_2H_5)_2$ • Di-[(methyldichlorosilyl)propyl] -diethylsilane	148—149 (2)	1.0830	1.4760	103.7	103.4	$C_{12}H_{28}Si_3Cl_4$	Found %: Cl 35.5, 35.1. Calculated %: Cl 35.6
14	$(Cl_3SiCH_2CH_2CH_2)_2$ 1,6-bis(Trichlorosilyl)hexane	131—132 (4)	1.3308	1.4760	74.8	74.7	$C_6H_{12}Si_2Cl_6$	Found %: Cl 60.5, 60.8. Calculated %: Cl 60.3
15	$[Cl_2(CH_3)SiCH_2CH_2CH_2]_2$ 1,6-bis(Methyldichlorosilyl)hexane	119—121 (3)	1.1310	1.4660	76.4	75.4	$C_8H_{18}Si_2Cl_4$	Found %: Cl 45.0, 46.1. Calculated %: Cl 45.3
16	$[Cl_2(C_2H_5)SiCH_2CH_2CH_2-]_2$ • 1,6-bis(Ethyldichlorosilyl)hexane	137—139 (2)	1.1273	1.4737	84.7	84.5	$C_{10}H_{22}Si_2Cl_4$	Found %: Cl 41.6, 41.5. Calculated %: Cl 41.7
17	$Cl(CH_3)(C_2H_5)SiCH_2CH_2(CH_3)(C_2H_5)SiOSi(CH_3)(C_2H_5)(CH=CH_2)$ • [(Methylethylchlorosilyl)ethyl]vinyldimethyldiethyl-disiloxane	101—103 (2)	0.9174	1.4490	94.5	94.4	$C_{13}H_{31}Si_3Cl$	Found %: Si 25.5, 25.8; C 48.6, 48.3; H 9.5, 9.7; Cl 10.6, 11.04. Calculated %: Si 26.0; C 48.3; H 9.7; Cl 11.0.

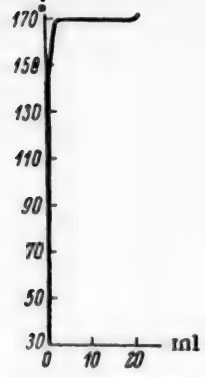


Fig. 2. 1,3-bis(Trimethylsilyl)propane distillation curve.

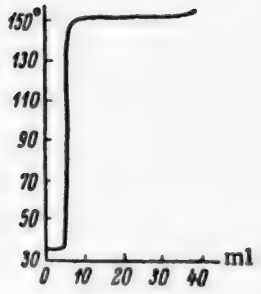


Fig. 3. 1,2-bis(Trimethylsilyl)ethane distillation curve.

Raman spectrum• ($\Delta\nu$ in cm^{-1}): 149 (1), 170 (4), 208 (very broad), 246 (3 broad), 268 (0), 316 (2), 578 (8), 603 (2), 615 (10), 691 (7 broad), 748 (0), 770 (0), 838 (2 broad), 870 (1), 910 (1 broad), 946 (0 broad), 980 (2 broad), 1025 (1 broad), 1145 (2 very broad), 1197 (2 broad), 1219 (2), 1248 (2), 1313 (1), 1356 (0), 1410 (4 broad), 1451 (0), 2860 (1), 2882 (1), 2903 (10), 2966 (10).

The methylation of $(CH_3)_3SiCH_2CH_2CH_2SiCl_2(CH_3)$ was run in conventional manner, and here we also obtained 1,3-bis(trimethylsilyl)propane in 89% yield. This compound had an analogous Raman spectrum and b.p. 171-172° (745 mm), $n^{20}D$ 1.4221, d^{20}_4 0.7566.

The methylation of $Cl_2(CH_3)SiCH_2CH_2Si(CH_3)Cl_2$ (38.5 g) was run in conventional manner, using the methylmagnesium chloride obtained from 24 g of magnesium. The yield of 1,2-bis(trimethylsilyl)ethane was 92% (Table 2, No. 6). The distillation curve (Fig. 3) indicates that only a single compound is present.

Raman spectrum, taken with a domestic ISP-31 spectrograph with a middle chamber ($\Delta\nu$ in cm^{-1}): 146 (1), 177 (6), 197 (3), 236 (6 broad), 310 (5 sharp), 604 (10), 640 (0.5), 681 (3), 696 (8), 782 (2), 846 (2), 867 (3 broad) 993 (2 sharp), 1102 (0), 1135 (2 broad), 1245 (7), 1257 (2), 1319 (1), 1355 (0), 1383 (1), 1411 (6), 2838 (1), 2668 (3), 2898 (10), 2956 (10).

The spectrum coincides with the spectrum of the 1,2-bis(trimethylsilyl)ethane given in [12]. Literature data [6] for 1,2-bis(trimethylsilyl)ethane: b.p. 150.5-151.0°, $n^{20}D$ 1.4194, d^{20}_4 0.7532; for 1,1-bis(trimethylsilyl)ethane: b.p. 159°, $n^{20}D$ 1.4322, d^{20}_4 0.7808.

1-Methyldiacetoxysilyl-2-ethyldiacetoxysilylethane (Table 2, No. 7). A mixture of 11 g (0.04 mole) of 1-(dichloromethylsilyl)-2-(dichloroethyl)ethane and 25 g (0.25 mole) of acetic anhydride was refluxed for 8 hr, in which connection the temperature dropped from 99° to 90° within 30 min after the start of heating and remained at this level to the end of the experiment. After distilling off the low-boiling components up to 137° the residue was fractionated in vacuo, where we collected the fraction with b.p. 167-169° at 2 mm to give 14.2 g of crystals with m.p. 34.5-35°. Based on the taken tetrachloride, the yield was 95%.

1,2-bis(Methyldiethoxysilyl)ethane (Table 2, No. 8). To 25.6 g (0.1 mole) of 1,2-bis(dichloromethylsilyl)-ethane and 32 g (0.405 mole) of pyridine in 200 ml of absolute benzene was added 19.3 g (0.42 mole) of ethanol in 10 min, with stirring. The reaction mixture was stirred for another 3 hr, separated from the precipitate, and the latter was washed with benzene. The benzene was removed by distillation. Fractionation of the residue in vacuo gave 14 g of colorless oil with b.p. 79-80° (1.5 mm). Yield 48%, based on taken tetrachloride.

SUMMARY

1. It was established that when trichlorosilane or methyldichlorosilane adds to the double bond of organosilicon compounds containing either the vinyl or the allyl radical, and also to 1,5-hexadiene, in the presence of chloroplatinic acid, the chlorosilyl or the alkylchlorosilyl group adds to the most hydrogenated carbon atom.

•An analogous spectrum for 1,3-bis(trimethylsilyl)propane is given in [12].

2. Some new members of α,ω-polychlorodisilanes containing hydrocarbon, silicohydrocarbon, and hydrocarbonsiloxane bridges were synthesized.

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SYNTHESIS AND PROPERTIES OF SALTS OF ACIDS AND OF SULFO ESTERS OF ALCOHOLS WITH ALKYLAROMATIC HYDROPHOBIC RADICALS

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The salts of straight-chain aliphatic acids of composition C_{10}-C_{20} and the salts of sulfo esters of straight-chain alcohols of composition C_{10}-C_{18} have been extensively studied for their surface-active and detergent properties [1], and these substances, as is known, find wide use in the national economy. Together with them, the alkylbenzenesulfonates with branched alkyl chains have earned a wide reputation as surface-active agents. At the same time, the properties of salts of acids and of sulfo esters of alcohols [2, 3] having an iso structure have received very little study, and have remained completely unstudied for compounds having an alkylaromatic hydrophobic radical. The purpose of the present investigation was to synthesize and study the surface-active properties of individual sodium salts of acids and of sulfo esters of alcohols, in which structurally similar alkylphenyl chains function as the hydrophobic radical. We synthesized two types of compounds: $R\text{-}C_6H_4\text{-}C(CH_3)_2CH_2X$ and $(CH_3)_2C_6H_3C(CH_3)_2CHX$, where X = COONa and $-OSO_2ONa$.

The synthesis of these compounds did not present any great difficulties, since we had already made a study of the chloroalkylation of monoalkylbenzenes with methallyl chloride [4], where, depending on the conditions, the yield of alkylation products ranged from 64 to 98%. By oxidizing these alkylates it was established that they contain approximately 85-90% of the p-isomer, while in the case of the chloroalkylation of tert-butylbenzene we were able to isolate the pure p-isomer. The chloroalkylation of o-, m-, and p-xylene was run in a similar manner. In all cases, as analysis of the infrared spectra revealed, the main products obtained here are the 1,2,4-substituted benzenes in 53-77% yields. The condensation of tetralin with methallyl chloride gave β-(chloro-tert-butyl)tetralin (84% yield).

Reaction of the organomagnesium compounds prepared from the condensation products of the mono- and dialkylbenzenes with methallyl chloride with oxygen gave the alcohols (55-70% yield), while reaction with carbon dioxide gave the acids (approximately 60% yield). From the acids we prepared the sodium salts, while from the alcohols we prepared the sodium salts of the sulfo esters.

$$R\text{—}C_6H_4\text{—}C(CH_3)_2CH_2MgCl \xrightarrow{O_2} R\text{—}C_6H_4\text{—}C(CH_3)_2CH_2OH \xrightarrow[NaOH]{ClSO_3OH} \rightarrow R\text{—}C_6H_4\text{—}C(CH_3)_2CH_2OSO_2ONa$$

$$R\text{—}C_6H_4\text{—}C(CH_3)_2CH_2MgCl \xrightarrow{CO_2} R\text{—}C_6H_4\text{—}C(CH_3)_2CH_2COOH \xrightarrow{NaOH} \rightarrow R\text{—}C_6H_4\text{—}C(CH_3)_2CH_2COONa$$

The properties of the obtained alcohols and acids are given in Table 1.

TABLE 1

Compound No.	Formula and name of compound	Yield (in %)	Temperature: boiling point (pressure in mm)	Temperature: melting point	d_4^{20}	n_D^{20}	MR_D: found	MR_D: calculated	Found (%): C	Found (%): H	Calculated (%): C	Calculated (%): H
(I)	$C_6H_5C(CH_3)_2CH_2OH$ * 2-Methyl 2-phenylpropanol	68	115—117° (20)	—	0.9969	1.5257	46.23	46.57	—	—	—	—
(II)	$CH_3C_6H_4C(CH_3)_2CH_2OH$ 2-Methyl-2-tolylpropanol	54	116—117 (12)	—	0.9817	1.5226	51.06	51.22	80.35, 80.43	9.91, 9.92	80.45	9.97
(III)	$C_2H_5C_6H_4C(CH_3)_2CH_2OH$ 2-Methyl 2-(ethylphenyl)propanol	71.7	119—121 (6)	—	0.9692	1.5182	55.75	55.88	80.17, 80.22	10.10, 10.11	80.80	10.18
(IV)	$(CH_3)_2CHC_6H_4C(CH_3)_2CH_2OH$ 2-Methyl-2-cumenylpropanol	60	—	59.5—60°	—	—	—	—	80.91, 80.95	10.30, 10.31	81.19	10.49
(V)	$2,4\text{-}(CH_3)_2C_6H_3C(CH_3)_2CH_2OH$ 2-Methyl-2-(2,4-dimethylphenyl)-propanol	55	90—92 (2)	—	0.9853	1.5312	55.99	55.88	80.77, 80.84	10.20, 10.11	80.80	10.18
(VI)	$3,4\text{-}(CH_2)_4C_6H_3C(CH_3)_2CH_2OH$ 2-Methyl-2-(β-tetralyl)propanol	65	118—119 (1)	—	1.0284	1.5500	63.29	63.11	82.26, 82.10	9.72, 9.73	82.30	9.86
(VII)	$C_6H_5C(CH_3)_2CH_2COOH$ * 2-Methyl-2-phenylbutanoic acid	63	—	58—59	—	—	—	—	—	—	—	—
(VIII)	$CH_3C_6H_4C(CH_3)_2CH_2COOH$ 2-Methyl-2-tolylbutanoic acid	65	—	74.5—75.5	—	—	—	—	74.89, 75.13	8.44, 8.56	74.98	8.39
(IX)	$C_2H_5C_6H_4C(CH_3)_2CH_2COOH$ 2-Methyl-2-(ethylphenyl)butanoic acid	65	—	72—73	—	—	—	—	75.97, 75.90	8.94, 8.90	75.70	8.79
(X)	$(CH_3)_2CHC_6H_4C(CH_3)_2CH_2COOH$ 2-Methyl-2-cumenylbutanoic acid	68	—	60—61	—	—	—	—	76.08, 76.23	9.04, 9.18	76.32	9.15
(XI)	$n\text{-}(CH_3)_3CC_6H_4C(CH_3)_2CH_2COOH$ 2-Methyl-2-(p-tert-butylphenyl) butanoic acid	77	—	115	—	—	—	—	77.12, 76.92	9.52, 9.51	77.00	9.47
(XII)	$3,4\text{-}(CH_2)_4C_6H_3C(CH_3)_2CH_2COOH$ 2-Methyl-2-(β-tetralyl)butanoic acid	67	—	88	—	—	—	—	76.82, 76.89	8.58, 8.72	77.12	8.68
(XIII)	$2,4\text{-}(CH_3)_2C_6H_3C(CH_3)_2CH_2COOH$ 2-Methyl-2-(2,4-dimethylphenyl) butanoic acid	60	—	75—76	—	—	—	—	76.18, 76.08	8.78, 8.73	75.70	8.79

*Obtained earlier by Whitmore and co-workers [5].

TABLE 2

Structure of salt	Detergency (concentration of compound 0.25%)	Surface tension (dynes/cm) at concentration (in %)			
		0.5	0.25	0.125	0.063
$C_6H_5C(CH_3)_2CH_2COONa$	3.5	71.1	72.5	72.8	72 8
$CH_3C_6H_4C(CH_3)_2CH_2COONa$	3.0	57.3	62.4	68.8	71.5
$C_2H_5C_6H_4C(CH_3)_2CH_2COONa$	3.0	59.6	62.5	67.2	70.2
$(CH_3)_2CHC_6H_4C(CH_3)_2CH_2COONa$	3.7	45.9	51.9	56.8	62.2
$2,4\text{-}(CH_3)_2C_6H_3C(CH_3)_2CH_2COONa$	2.6	63.5	66.8	70.8	71.1
$C_6H_5C(CH_3)_2CH_2OSO_2ONa$	2.4	40.6	43.9	53.2	56.5
$CH_3C_6H_4C(CH_3)_2CH_2OSO_2ONa$	3.2	72.8	72.8	72.8	72.8
$C_2H_5C_6H_4C(CH_3)_2CH_2OSO_2ONa$	3.0	60.5	65.5	69.8	71.1
$(CH_3)_2CHC_6H_4C(CH_3)_2CH_2OSO_2ONa$	3.4	57.8	64.8	69.8	71.1
Hard water	2.7				
$n\text{-}CH_3(CH_2)_8COONa$	—	32.6	44.5	63.6	70.9
$n\text{-}CH_3(CH_2)_{10}COONa$	—	25.5	38.0	57.8	—
$n\text{-}CH_3(CH_2)_{12}COONa$	—	34.9	37.5	46.7	—
$n\text{-}CH_3(CH_2)_{10}CH_2OSO_3Na$	—	39.1	36.7	—	44

The surface tension and the detergency were determined for most of the acid salts and the salts of the sulfo esters of the alcohols. The surface tension of the solutions (in distilled water) was determined at 20° in the P. A. Rebinder apparatus by the method of the greatest bubble pressure; the detergency was determined using artificially soiled samples of cotton cloth (calico 101, GOST 7617-55). The washing was done in hard water (15° German) in a launderometer at 40°. The detergency was expressed by the difference in the photometer readings when the cloth samples were photometered before and after washing. The photometering was done with a Zeiss leucometer. The obtained results are given in Table 2.

It is possible to conclude from these data that a partial replacement of the aliphatic carbon atoms in the molecule by the aromatic ring causes a sharp decrease in both the surface tension and detergency of the investigated compounds. It is interesting to mention that even in the case of $C_6H_5C(CH_3)_2CH_2COONa$ and $(CH_3)_3CC_6H_4C(CH_3)_2CH_2COONa$, differing substantially in molecular weight, the detergency is nearly the same (3.5 and 3.7, respectively), although the surface tension is quite different.

EXPERIMENTAL

Alcohols (I-VI). All of the alcohols and the sodium salts of their sulfo esters were obtained by the same method, using nearly the same molar ratio of the reactants in all of the experiments. We will describe a typical experiment. To 60 g (2.5 g-at) of magnesium immersed in ether was added 273 g (1.5 moles) of chloro-tert-butyltoluene in 4 hr. After all of the chloride had been added, the flask contents were stirred at ether boil for 1.5 hr, after which the flask was cooled and the addition of oxygen was begun at 3-5°. At the end of reaction the reaction mass was decomposed with water and dilute sulfuric acid. The ether layer was vacuum distilled to yield 134 g of 2-methyl-2-tolyl-1-propanol. The properties and yields of the alcohols are given in Table 1. The melting point of 2-methyl-2-cumenyl-1-propanol was determined after its recrystallization from cyclohexane.

Sodium salts of sulfo esters. To 111 g (1.4 mole) of pyridine was added 75.7 g (0.65 mole) of chlorosulfonic acid. Then 81 g (0.5 mole) of 2-methyl-2-tolyl-1-propanol was added at one time to the obtained solid complex. The vigorously stirred reaction mixture was heated at 70° until a homogeneous mass was obtained. The heating was then continued for another hour, 10 g of ice was added, and then the flask contents were neutralized with 48% NaOH and treated with 100 ml of hot water. The organic layer was separated from the water layer and then evaporated in vacuo at 60° to give 130 g of crystalline product. The crystals were washed with ether, recrystallized twice from hot water, and analyzed.

Found %: C 46.17, 46.28; H 6.01, 5.99; S 5.61, 5.35; ash 25.68, 25.67. $C_{12}H_{15}O_4SNa \cdot H_2O$. Calculated %: C 46.46; H 6.02; S 5.63; ash 25.00.

Acids (VII-XIII). The acids and their salts were also obtained by a single procedure. Carbon dioxide was passed for 2 hr at 5-10° through the Grignard reagent prepared from 147 g (0.75 mole) of (chloro-tert-butyl)-ethylbenzene and 27.4 g of magnesium. Then 300 g of solid carbon dioxide was added in portions over a period of 3 hr. The reaction mass was decomposed with 25% sulfuric acid, and the ether solution was vacuum distilled to yield 100 g of 2-methyl-2-(ethylphenyl)butanoic acid with b.p. 168-171° (6 mm). The melting points of the acids were determined after their recrystallization from aqueous alcohol.

The sodium salts of the acids were obtained by refluxing the acids with 10% NaOH solution in alcohol. The acids were taken in slight excess with respect to the alkali; to remove the excess acid the salts were washed with ether.

SUMMARY

1. We were the first to synthesize the salts of acids and of the sulfo esters of alcohols of composition C_{10}–C_{15}, in which a part of the alkyl chain was replaced by the benzene ring. It was established that this replacement sharply lowers both the surface-active, and especially, the detergent properties of the compounds.

2. It was established that the surface-active properties are close for salts of acids and of sulfo esters of alcohols that have approximately the same molecular weight and are structurally similar.

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THE STRUCTURE OF FORMAZANS.

STUDY OF THE MAGNETIC SUSCEPTIBILITY OF THE COMPLEXES OF COPPER, COBALT, AND NICKEL WITH FORMAZANS

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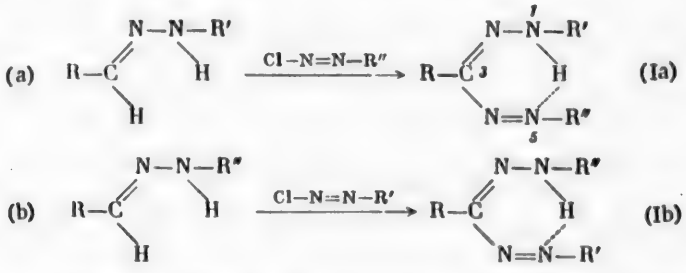
The structure of the formazans has been discussed by many authors [1]. As early as 1894 von Pechmann [2], in studying the reactions of the formazans, came to the conclusion that formazans (Ia) and (Ib), obtained by two possible routes, are identical.



From these data it is possible to conclude that formazans in the crystalline state exist in only one of the possible tautomeric forms, independent of the mode of synthesis. At the same time it is known that the acetylation of formazans yields acetyl compounds of variable tautomeric form [2].

The manifestation of tautomerism by formazans in cleavage reactions was shown when a study was made of unsymmetrically substituted 1,3,5-triphenylformazans labeled with C^{14} [3]. In the case of symmetrically substituted formazans, i.e., when R' = R", the authors assume that it is possible for the mesomeric system to exist. It was shown earlier by Hunter and Roberts [4] that formazans have a chelate structure and are capable of forming complexes with certain metals. The identity of the formazans and the presence of intramolecular bonding gave the authors reason to assume the existence of (Ia) and (Ib) as a "resonance hybrid."

On the assumption that explaining the structural peculiarities of formazans by the presence of a "mesomeric system" or a "resonance hybrid" is unwarranted, we deemed it desirable to obtain additional experimental data regarding the structure of formazans by making a study of their infrared spectra and the magnetic properties of some of the complexes of formazans. For the infrared spectra the compounds were taken both in the crystalline state and in dioxane solution. The following formazans were studied: 1,3,5-triphenylformazan, 1-p-tolyl-3,5-diphenylformazan, and 1-p-chlorophenyl-3,5-diphenylformazan.* It proved that neither in the crystalline state nor in dioxane solution did one of the investigated formazans show clearly defined absorption bands in the 3400-2900 cm^{-1}

*The infrared spectra were taken jointly with L. F. Trefilova using an IRS-12 spectrometer.

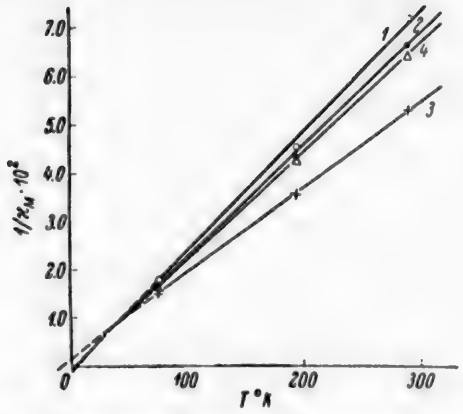


Fig. 1. Relation between the magnetic susceptibility of copper salts of formazans and the temperature. 1) bis(1,3,5-triphenylformazyl) copper; 2) bis(1-p-tolyl-3,5-diphenylformazyl) copper; 3) bis(1-p-chlorophenyl-3,5-diphenylformazyl)copper; 4) 1-o-carboxyphenyl-3,5-diphenylformazylcopper.

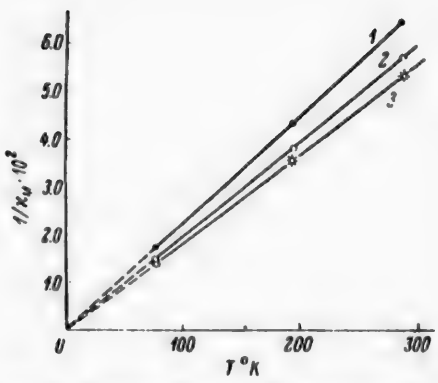
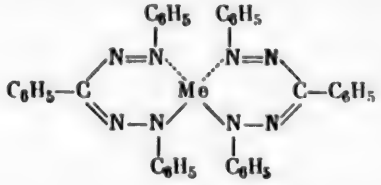


Fig. 2. Relation between the magnetic susceptibility of cobalt salts of formazans and the temperature. 1) bis(1,3,5-triphenylformazyl) cobalt; 2) bis(1-p-tolyl-3,5-diphenylformazyl) cobalt; 3) bis(1-p-chlorophenyl-3,5-diphenylformazyl)cobalt.

region (LiF prism), where the vibrations of the NH group appear. This is convincing evidence that the NH group in formazans is involved in the formation of a short and stable (see [5]) intramolecular hydrogen bond.

The identity of (Ia) and (Ib) because of this fact, and also the deep color of formazans, both suggest a continuous conjugation in the planar formazan ring with a quite level π-electron system. In this should lie the main reason for the stability of the hydrogen bond, functioning to close the six-membered ring. A similar postulation regarding the planar and even the "aromatic" character of this ring was made recently for the nickel complex of 1-o-carboxyphenyl-3,5-diphenylformazan [6]. To confirm these opinions we thought it of interest to study the magnetic properties of some of the complexes of formazans with Cu, Co, and Ni. Such a study could throw some light on the spatial arrangement of the atoms in the tetrazo ring.

Triphenylformazans not substituted in the o-position to the formazan chain form, as is known [4], complexes with Cu, Co, and Ni, in which one metal atom is linked to two formazan molecules.



Six electrons from two formazan molecules are involved in the formation of the bonds. In the case of the complex with Co^{2+} either a tetrahedral structure with $4s4p^3$ bonds or a tetragonal structure with $3d4s4p^2$ bonds could be expected, the magnetic moments of which are equal to 3.88 and 1.73 Bohr magnetons, respectively [7].

Figgis and Nyholm [8] have shown that all of the studied Co^{2+} complexes forming covalent bonds have a planar tetragonal structure. The magnetic moments of these compounds range from 2.1 to 2.9 Bohr magnetons. (The authors explain the high value of the magnetic moment when compared to the theoretical of 1.73 as due to a greater orbital component.)

Measuring the magnetic susceptibility of Ni^{2+} complexes makes it also possible to distinguish between the tetrahedral and the tetragonal structure, since in the first case the compounds are paramagnetic, while in the second case they are diamagnetic.

TABLE 1

Complexes of Formazans

Expt. No.	Name of complex	Empirical formula	Melting point		Nitrogen content (%)		Metal content (%)	
			found	literature	found	calculated	found	calculated
I	bis(1,3,5-Triphenylformazyl)copper	$C_{38}H_{30}N_8Cu$	159—160°	158° [4]	17.15	16.92	9.21	9.59
II	bis(1-p-tolyl-3,5-Diphenylformazyl) copper	$C_{40}H_{34}N_8Cu$	158—159	156 [4]	16.01	16.24	9.35	9.20
III	bis(1-p-Chlorophenyl-3,5-diphenylformazyl) copper	$C_{38}H_{28}N_8Cl_2Cu$	166—168	—	15.38	15.33	8.50	8.69
IV	1-o-Carboxyphenyl-3,5-diphenylformazylcopper	$C_{20}H_{14}O_2N_4Cu$	231 (with decompn.)	228 [13] (with decompn.)	13.60	13.80	15.47	15.65
V	bis(1,3,5-Triphenylformazyl)cobalt	$C_{38}H_{30}N_8Co$	227—228	228—230 [4]	17.28	17.04	9.11	8.96
VI	bis(1-p-tolyl-3,5-Diphenylformazyl) cobalt	$C_{40}H_{34}N_8Co$	236—237	238 [4]	16.37	16.35	8.61	8.59
VII	bis(1-p-Chlorophenyl-3,5-diphenylformazyl) cobalt	$C_{38}H_{28}N_8Cl_2Co$	184—185	—	15.19	15.44	8.03	8.11
VIII	bis(1,3,5-Triphenylformazyl)nickel	$C_{38}H_{30}N_8Ni$	306 (with decompn.)	300 [4] (with decompn.)	17.50	17.05	8.77	8.93
IX	bis(1-p-tolyl-3,5-Diphenylformazyl) nickel	$C_{40}H_{34}N_8Ni$	293 (with decompn.)	287 [4] (with decompn.)	16.42	16.35	8.42	8.56
X	bis(1-p-Chlorophenyl-3,5-diphenylformazyl) nickel	$C_{38}H_{28}N_8Cl_2Ni$	288 (with decompn)	—	15.12	15.44	7.85	8.08
XI	1-o-Carboxyphenyl-3,5-diphenylformazylnickel	$C_{20}H_{14}O_2N_4Ni$	275 (with decompn.)	270 [13] (with decompn.)	14.37	13.97	14.82	14.64

The complexes of divalent copper have one unpaired electron, and for this reason are paramagnetic. In this case it is possible to have both the tetragonal $2d4s4p^2$ and $4s4p^24d$ structures and the tetrahedral $4s4p^3$ structure. In this case measuring the magnetic susceptibility does not answer the question of the stereochemistry of the complex; however, it is possible to make an estimate by comparison with the analogous complexes of Co^{2+} and Ni^{2+}. As a result, a study of the magnetic properties of the complexes of Cu^{2+}, Co^{2+}, and Ni^{2+} with formazans makes it possible to decide whether the arrangement of the tetrazo ring is planar or nonplanar.

In this paper we prepared the complexes of cobalt, nickel, and copper with the following formazans: 1,3,5-triphenylformazan, 1-p-tolyl-3,5-diphenylformazan, 1-p-chlorophenyl-3,5-diphenylformazan, and 1-o-carboxyphenyl-3,5-diphenylformazan. [The three complexes (II), (VII) and (X) (Table 1) are new.]

The integral method of Guoy was used to determine the magnetic susceptibility of the complexes. The measurements were made at 77, 196, and 291° K by the method taken from the book by W. Klemm [9].

As can be seen from Figs. 1 and 2, within the studied temperature range the magnetic susceptibility of the copper salts of the formazans obeys the Curie—Weiss law, while the susceptibility of the analogous cobalt

TABLE 2

Magnetic Susceptibility of Complexes of Formazans With Copper, Cobalt, and Nickel (at a field intensity of 2260 oersteds)

Expt. No.	Name of compound	Temperature, °K	$\chi_g \cdot 10^6$	$\chi_M \cdot 10^6$	θ° K	μ effect (in Bohr magnetons)
I	bis(1,3,5-Triphenylformazyl) copper	293	1.55	1381	+5	1.81
		196	2.79	2197		
		77	8.00	5652		
II	bis(1-p-tolyl-3,5-Diphenyl-formazyl)copper	291	1.62	1494	+4	1.87
		196	2.80	2303		
		77	8.01	5900		
III	bis(1-p-Chlorophenyl-3,5-diphenylformazyl)copper	293	2.14	1900	−10	2.08
		196	3.35	2822		
		77	8.56	6637		
IV	1-o-Carboxyphenyl-3,5-diphenylformazylcopper	291	3.37	1557	+4	1.90
		196	5.22	2303		
		77	14.60	6116		
V	bis(1,3,5-Triphenylformazyl) cobalt	291	1.86	1572	0	1.93
		196	3.07	2365		
		77	8.58	5993		
VI	bis(1-p-tolyl-3,5-Diphenyl-formazyl)cobalt	291	2.08	1795	0	2.05
		196	3.34	2647		
		77	9.36	6773		
VII	bis(1-p-Chlorophenyl-3,5-diphenylformazyl)cobalt	291	2.11	1914	0	2.12
		196	3.39	2839		
		77	9.45	7237		
VIII	bis(1,3,5-Triphenylformazyl) nickel	291	−0.273	−199		
IX	bis(1-p-tolyl-3,5-Diphenyl-formazyl)nickel	291	−0.279	−209		
X	bis(1-p-Chlorophenyl-3,5-diphenylformazyl)nickel	291	−0.289	−230		
XI	1-o-Carboxy-3,5-diphenyl-formazylnickel	291	−0.283	−123		

compounds obeys the Curie law. In Table 2 we have given the specific magnetic susceptibilities of all of the investigated compounds, the molar magnetic susceptibilities, calculated with the proper correction for diamagnetism, and finally, the effective magnetic moments of the copper and cobalt atoms in their compounds with the formazans.

The obtained data indicate that the magnetic moments of the Co^{2+} complexes have values ranging from 1.93 to 2.12, i.e., they correspond to the tetragonal structure with $3d4s4p^2$ bonds. The magnetic moments of the nickel complexes are equal to zero; these complexes are diamagnetic, and consequently, they have the tetragonal structure with $3d4s4p^2$ bonds. The magnetic moments of the Cu^{2+} complexes have values ranging from 1.81 to 2.08, and probably the same as the Ni^{2+} and Co^{2+} complexes, these complexes have a planar structure.

The given measurements of the magnetic susceptibility make it possible to conclude that the tetrazo ring in the complexes has a planar structure. Consequently, it can be assumed that the conjugated system in the tetrazo ring of the formazan is also planar in the stable form.• The deep color of formazans and the stability of the hydrogen bond closing the six-membered ring are found to be related to this.

•It must be assumed that the benzene radicals are also found in the same plane as the tetrazo ring, which assures a maximum conjugation of the bonds of all of the molecules.

EXPERIMENTAL

To obtain the complexes needed for the magnetic measurements, we used the magnetically pure acetates of the metals. Copper acetate was recrystallized 3 times from doubly distilled water containing several drops of freshly distilled acetic acid. Cobalt acetate was prepared by the method of [10] through the hydroxide, with subsequent refluxing in anhydrous alcohol with glacial acetic acid. The obtained acetate was recrystallized twice from doubly distilled water containing several drops of glacial acetic acid, and was dried at 110-120° for 6 hr. Nickel acetate was prepared from nickel nitrate free of cobalt; a solution of 14.5 g of $Ni(NO_3)_2$ in 500 ml of water was neutralized with 4.1 g of NaOH in 50 ml of water. The nickel hydroxide precipitate was washed by decantation with distilled water for 4 days, after which it was filtered and dried at 60°. The dry product was treated with 12 g of glacial acetic acid and 50 ml of anhydrous alcohol. Then the mixture was heated under reflux for 2 hr, after which the precipitate was filtered and dried. The dry nickel acetate was dissolved with heating in the minimum amount of dilute acetic acid, and after cooling was precipitated by the addition of 96% alcohol. The obtained nickel acetate was dried at 110° for 2-3 hr. The magnetic susceptibility of the starting acetates agreed with the literature data [11, 12].

The complexes of 1,3,5-triphenylformazan, 1-p-tolyl-3,5-diphenylformazan and 1-p-chlorophenyl-3,5-diphenylformazan with Cu, Co, and Ni were obtained by the method of [4], i.e., by mixing hot solutions of the formazans in acetone with solutions of the appropriate acetates in 50% alcohol. The complexes of Cu and Ni with 1-o-carboxyphenyl-3,5-diphenylformazan were obtained by the method of [13]. The preparation of the complexes not reported in the literature is given below.

bis(1-p-Chlorophenyl-3,5-diphenylformazyl)copper (III). A hot solution of 0.35 g (0.001 mole) of 1-p-chlorophenyl-3,5-diphenylformazan, m.p. 173-174°, in 30 ml of acetone was mixed with a hot solution of 0.2 g of copper acetate in 5 ml of 50% alcohol. The mixture after stirring was allowed to stand overnight. The obtained precipitate of the complex was filtered, washed with 0.1 N hydrochloric acid and alcohol, and dried at 110°. The complex was obtained as black plates with a metallic luster, m.p. 155°, and soluble in acetone, ether, and dioxane. Yield 0.2 g (60%).

bis(1-p-Chlorophenyl-3,5-diphenylformazyl)cobalt (VII). A hot solution of 0.35 g of 1-p-chlorophenyl-3,5-diphenylformazan in 30 ml of acetone was mixed with a solution of 0.15 g of anhydrous cobalt acetate in 2 ml of water. After heating the mixture on the water bath for 2 hr and then cooling, the obtained precipitate of the complex was filtered, washed with warm alcohol and 0.1 N hydrochloric acid, and dried at 110°. Black crystals with a metallic luster, appearing as dark ruby rhombic crystals under the microscope, with m.p. 183-184°, and readily soluble in acetone, ether, and dioxane. Yield 0.2 g (60%).

bis(1-p-Chlorophenyl-3,5-diphenylformazyl) nickel (X). Obtained in the same manner as complex (VII). From 0.35 g of the formazan and 0.15 g of anhydrous nickel acetate we obtained 0.3 g (90%) of black needles with a metallic luster, not melting up to 250°, and readily soluble in ether, acetone, and dioxane. The analyses of the obtained complexes are given in Table 1.

SUMMARY

1. The magnetic susceptibilities of the complexes of 1,3,5-triphenylformazan, 1-p-tolyl-3,5-diphenylformazan, 1-p-chlorophenyl-3,5-diphenylformazan, and 1-o-carboxyphenyl-3,5-diphenylformazan with cobalt, nickel, and copper were measured, and the infrared spectra of the indicated formazans were taken. The magnetic measurements revealed that the structure of all of the investigated complexes corresponds to a planar arrangement of the formazyl group.

2. The absence of absorption bands for the NH group in the infrared spectra of the formazans and the magnetic properties of their complexes with Cu, Co, and Ni both indicate that the tetrazo ring in the formazan molecule is planar, and apparently has an aligned electron system involving a stable hydrogen bond, functioning to close the six-membered ring.

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STUDIES IN THE FURAN SERIES

V.• SYNTHESIS OF N-(TRICHLOROMETHYLMERCAPTO)IMIDE DERIVATIVES OF 3,6-ENDOXOHEXAHYDROPHTHALIC ACID

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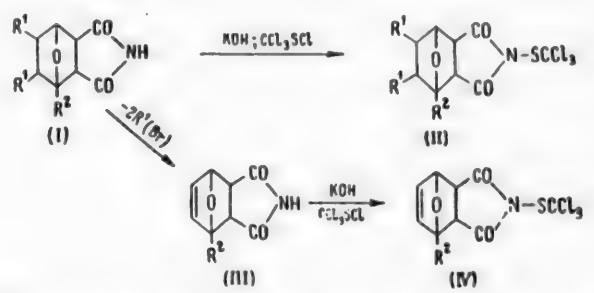
It was shown by Kittleson [1] in 1951 that compounds containing the >N-SCCl$_3$ group, as exemplified by the N-trichloromethylmercapto-imides,-oxazolidinediones [2],and -thiazolidinediones [3], can be used as fungicides, insecticides and germicides. One of the compounds in this series, the N-(trichloromethylmercapto)imide of Δ^4-tetrahydrophthalic acid, is manufactured in the United States under the name of "Captan" or "Orthocide 75". The high fungicidal activity, broad spectrum of action, and stability of the compound make it one of the better fungicides. Since the literature on the biological action of "Captan" is quite voluminous, we will only mention here that it is used against the brown rot of apples and plums [4], to protect fruit and citrus trees and strawberry plants [5], and also in the preparation of germicidal soap [6].

It is also known that 3,6-endoxohexahydrophthalic anhydride and some of its derivatives find use as herbicides, insecticides, and especially as defoliants [7, 8]; the sodium salt of 3,6-endoxohexahydrophthalic acid under the name of "Endothal" is used as a defoliant and desiccant in cotton fields [9, 10].

Since the activity of N-trichloromethylmercapto compounds is determined by the presence of the -S-CCl$_3$ group [11], it seemed of interest to obtain compounds containing both this group and the 3,6-endoxocyclohexane group, and with this in mind we synthesized several N-(trichloromethylmercapto)imides of 3,6-endoxohexahydrophthalic acid and related acids.

From the brief patent information [1, 12] it is known that N-(trichloromethylmercapto)imides can be obtained by the reaction of perchloromethyl mercaptan with salts of the imide in a neutral solvent or with an aqueous alkaline solution of the imide at low temperature (0-30°), in order to avoid hydrolysis of the imides.



(I, II): $R^1=R^2=H$; $R^1=Cl$, $R^2=H$; $R^1=Cl$, $R^2=CH_3$; $R^1=Br$, $R^2=H$; $R^1=H$, $R^2=CH_3$; $R^1=H$, $R^2=CH_2OCOCH_3$; (III, IV): $R^2=H$;

•For Communication IV see: Doklady Akad. Nauk SSSR 126, 806 (1959).[See C. B. translation, p. 425.]

We used both variations and established that the reaction of perchloromethyl mercaptan with an aqueous alkaline solution of the imide of 3,6-endoxohexahydrophthalic acid or its derivatives leads to obtaining the corresponding N-trichloromethylmercapto derivatives of this series in high yield (80-90%) and makes it possible to eliminate the superfluous step of obtaining the salt of the imide.

EXPERIMENTAL •

1. Synthesis of anhydrides. Exo-4,5-dichloro-3,6-endoxohexahydrophthalic anhydride. With stirring and ice cooling, a stream of dry chlorine was passed into a suspension of 33.2 g (0.2 mole) of 3,6-endoxo-Δ^4-tetrahydrophthalic anhydride in 500 ml of methyl acetate until saturated, after which the mixture was allowed to stand at 0-5° for 2 hr, and then the methyl acetate was vacuum distilled to incipient crystallization of the residue. An equal volume of petroleum ether was added to the residue, and after standing for 0.5 hr the precipitate was filtered. The yield was 36 g; another 9 g was isolated from the mother liquor. Total yield 45 g (95%); m.p. 165-165.5° (from a mixture of acetone and petroleum ether).

Found %: C 40.43, 40.54; H 2.54, 2.71. $C_8H_6O_4Cl_2$. Calculated %: C 40.53; H 2.55.

4,5-Dichloro-3-methyl-3,6-endoxohexahydrophthalic anhydride. In the same manner as described above, from 36.0 g (0.2 mole) of 3-methyl-3, 6-endoxo-Δ^4-tetrahydrophthalic anhydride (m.p. 84°) we obtained 46 g (92%) of product; m.p. 153-153.5° (from a mixture of methyl acetate and petroleum ether).

Found %: C 42.89, 42.95; H 3.37, 3.49. $C_9H_8O_4Cl_2$. Calculated %: C 43.05; H 3.21.

2. Synthesis of imides. All of the imides, except the earlier described imides of exo-3,6-endoxo-Δ^4-tetrahydrophthalic (m.p. 160-161°) and exo-4,5-dibromo-3,6-endoxohexahydrophthalic (m.p. 219-221°) acids [13], were synthesized in the following manner.

The appropriate anhydride was added with stirring to 25% ammonia solution, after which the mixture was heated to 100°, and then additional ammonia was added if needed until a clear solution was obtained, which was then evaporated to dryness. The residue was heated slowly to 240-250° and then kept at this temperature for 15 min. That melt was cooled, and then: a) it was dissolved in a small volume of hot water, boiled with carbon, and filtered; the imide crystallized on cooling; or b) the residue was dissolved in hot acetone, carbon was added, the solution filtered, the filtrate evaporated to incipient crystallization, and the residue diluted with three volumes of petroleum ether; the imide was filtered and recrystallized from suitable solvent.

Imide of exo-3,6-endoxohexahydrophthalic acid. Using method "a", from 50.4 g (0.3 mole) of 3, 6-endoxohexahydrophthalic anhydride (m.p. 116-117°) [14] we obtained 45.5 g (90%) of product; m.p. 180-181°.

Literature data [15]: m.p. 181°.

Imide of exo-4,5-dichloro-3,6-endoxohexahydrophthalic acid. Using method "b", from 23.7 g (0.1 mole) of 4,5-dichloro-3,6-endoxohexahydrophthalic anhydride we obtained 19.8 g (84%) of product; m.p. 215-216° (from a mixture of acetone and petroleum ether); after vacuum sublimation, m. p. 215.5-216°.

Found %: C 40.73, 40.89; H 2.98, 2.97; N 5.77, 5.80. $C_8H_7O_3NCl_2$. Calculated %: C 40.69; H 2.99; N 5.93.

Imide of 3-methyl-3,6-endoxohexahydrophthalic acid. Using method "a", from 18.2 g (0.1 mole) of 3-methyl-3,6-endoxohexahydrophthalic anhydride (m.p. 105-106°) [16] we obtained 16.6 g (92%) of the imide; m.p. 158.5-159.5° (from water).

Found %: C 59.56, 59.69; H 6.08, 5.98; N 7.82, 7.74. $C_9H_{11}O_3N$. Calculated %: C 59.65; H 6.12; N 7.78.

Imide of 4,5-dichloro-3-methyl-3,6-endoxohexahydrophthalic acid. Using method "b", from 25.1 g (0.1 mole) of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic anhydride we obtained 20.2 g (81%) of the imide ; m.p. 214-215° (from alcohol).

Found %: C 43.41, 43.43; H 3.53, 3.62; N 5.54, 5.67. $C_9H_9O_3NCl_2$. Calculated %: C 43.22; H 3.62; N 5.60.

• The melting points of all of the compounds were determined in sealed capillaries and are uncorrected.

Imide of 3-acetoxymethyl-3,6-endoxohexahydrophthalic acid. Twenty-four grams (0.1 mole) of 3-acetoxymethyl-3,6-endoxohexahydrophthalic anhydride (m.p. 130°) [17] was dissolved with heating in 300 ml of benzene, and then a stream of ammonia was passed through the solution until saturated. The white ammonium salt of the polyamide of 3-acetoxymethyl-3,6-endoxohexahydrophthalic acid was filtered and then heated slowly to 200-210°, where it was kept for 15 min, and then it was worked up by method "b". We obtained 18.9 g (79%) of the imide; m.p. 163-164° (from water).

Found %: C 55.34, 55.32; H 5.61, 5.57; N 5.77, 5.74. $C_{11}H_{13}O_5N$. Calculated %: C 55.23; H 5.48; N 5.85.

3. Synthesis of N-(trichloromethylmercapto)imides from the imide salt. N-(Trichloromethylmercapto) imide of exo-3,6-endoxohexahydrophthalic acid. A suspension of 4.2 g (0.025 mole) of the imide of 3,6-endoxohexahydrophthalic acid in 35 ml of anhydrous alcohol was heated to 60°, and then a solution of 1.5 g of KOH in 30 ml of anhydrous alcohol heated to 60° was added at one time with stirring. Solution occurred immediately, and after several minutes a copious precipitate of the potassium salt of the imide began to deposit. The mixture was cooled, and the precipitate was filtered and air-dried. The yield was nearly quantitative.

In a flask fitted with a stirrer, reflux condenser, and dropping funnel was suspended 3.1 g (0.015 mole) of the potassium salt of the imide in 20 ml of dry benzene, and then a solution of 2.8 g of perchloromethyl mercaptan in 5 ml of benzene was added dropwise. The mixture warmed up and a precipitate of potassium chloride deposited. The mixture was refluxed for 1 hr, filtered hot, and cooled. We obtained 4.1 g (90%) of the imide; m.p. 157.5-158° (from benzene).

Found %: C 34.10, 34.08; H 2.41, 2.54; N 4.35, 4.38. $C_9H_8O_3NSCl_3$. Calculated %: C 34.13; H 2.54; N 4.42.

N-(Trichloromethylmercapto)imide of exo-4,5-dibromo-3,6-endoxohexahydrophthalic acid. In the same manner as described above, from 8.1 g (0.025 mole) of the imide in 100 ml of anhydrous alcohol and 1.7 g of KOH in 50 ml of anhydrous alcohol we obtained 8.5 g of the potassium salt of the imide. To a suspension of 7.28 g (0.02 mole) of the salt in 50 ml of benzene was added 3.8 g of perchloromethyl mercaptan with stirring, the mixture refluxed for 2 hr, the benzene removed by distillation, and the dry residue extracted with acetone. The acetone was evaporated to incipient crystallization, and the residue was diluted with three volumes of petroleum ether. We obtained 8.4 g (89%) of the imide; m.p. 184-185° (from alcohol).

Found %: C 22.81, 22.90; H 1.29, 1.32; N 2.90, 3.01. $C_9H_6O_3NSCl_3Br_2$. Calculated %: C 22.78; H 1.28; N 2.95.

4. Synthesis of N-(trichloromethylmercapto)imides in aqueous alkaline solution. The imide (0.1 mole) was added with stirring to a solution of 6.3 g (0.11 mole) of KOH in 100 ml of water and the stirring continued until solution was obtained. Then 18.6 g (0.1 mole) of perchloromethyl mercaptan was added dropwise in 1 hr, the mixture stirred for another 2 hr, and the precipitate filtered and recrystallized. In the case of the halogen-containing imides (due to the lower solubility of the imide salt), the imides were added to a solution of 6.3 g of KOH in 250 ml of water.

N-(Trichloromethylmercapto)imide of exo-3,6-endoxohexahydrophthalic acid. From 16.7 g (0.1 mole) of the imide we obtained 28.0 g (88%) of product; m.p. 157.5-158° (from benzene); the mixed melting point with the earlier obtained compound was not depressed.

N-(Trichloromethylmercapto)imide of exo-3,6-endoxo-Δ^4-tetrahydrophthalic acid. From 16.5 g (0.1 mole) of the imide we obtained 26.1 g (83%) of product; m.p. 132-132.5° (from alcohol).

Found %: C 34.54, 34.33; H 2.03, 2.11; N 4.42, 4.55. $C_9H_6O_3NSCl_3$. Calculated %: C 34.36; H 1.92; N 4.45.

N-(Trichloromethylmercapto)imide of exo-4,5-dibromo-3,6-endoxohexahydrophthalic acid. From 32.5 g (0.1 mole) of the imide we obtained 41.3 g (87%) of product; m.p. 184-185° (from alcohol); the mixed melting point with the earlier obtained compound was not depressed.

N-(Trichloromethylmercapto)imide of exo-4,5-dichloro-3,6-endoxohexahydrophthalic acid. From 23.6 g (0.1 mole) of the imide we obtained 31.2 g (81%) of product; m.p. 169.5-170° (from alcohol).

Found %: C 28.13, 28.22; H 1.70, 1.67; N 3.65, 3.55. $C_9H_6O_3NSCl_5$. Calculated %: C 28.03; H 1.57; N 3.63.

N-(Trichloromethylmercapto)imide of 3-methyl-3,6-endoxohexahydrophthalic acid. From 18.1 g (0.1 mole) of the imide we obtained 28.0 g (85%) of product; m.p. 148.5-149° (from a mixture of benzene and petroleum ether).

Found %: C 36.42, 36.48; H 3.17, 3.20; N 4.24, 4.15. $C_{10}H_{10}O_3NSCl_3$. Calculated %: C 36.32; H 3.05; N 4.24.

N-(Trichloromethylmercapto)imide of 4,5-dichloro-3-methyl-3,6-endoxohexahydrophthalic acid. From 25.0 g (0.1 mole) of the imide we obtained 33.2 g (83%) of product; m.p. 214-215° (from toluene).

Found %: C 30.16, 30.25; H 1.84, 2.02; N 3.41, 3.53. $C_{10}H_8O_3NSCl_5$. Calculated %: C 30.06; H 2.02; N 3.50.

N-(Trichloromethylmercapto)imide of 3-acetoxymethyl-3,6-endoxohexahydrophthalic acid. From 24 g (0.1 mole) of the imide we obtained 30.2 g (78%) of product; m.p. 158° (from alcohol).

Found %: C 37.22, 37.30; H 3.13, 3.26; N 3.67, 3.69. $C_{12}H_{12}O_5NSCl_3$. Calculated %: C 37.11; H 3.09; N 3.60.

SUMMARY

Based on 3,6-endoxo-Δ^4-tetrahydrophthalic anhydride, we synthesized a number of N-(trichloromethylmercapto)imide derivatives of 3,6-endoxohexahydrophthalic acid.

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*Chemical Abstracts.

CHEMISTRY OF SELENOPHENE

XXV. 4-NITRO-2-ACETOSELENOPHENE AND 4-NITRO-2-SELENOPHENECARBOXYLIC ACID

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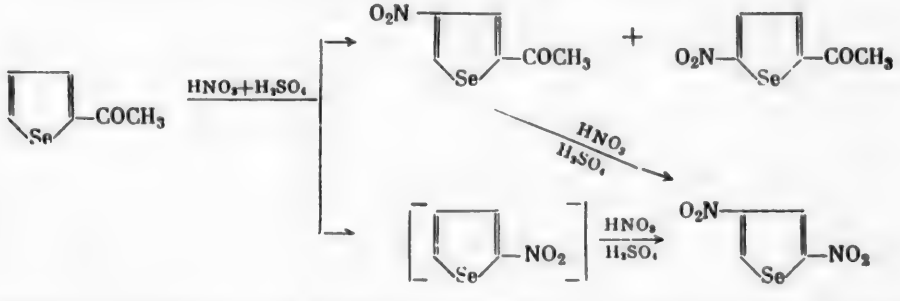
In our previous paper [1] we described obtaining 5-nitro-2-acetoselenophene by the reaction of 5-nitro-2-selenophenecarbonyl chloride with ethoxymagnesiummalonic ester. When the nitration of 2-acetoselenophene was examined we established that the nitration product—a mixture of 4- and 5-nitro-2-acetoselenophene—is obtained in very low yield (9.5%) when the reaction is run with fuming nitric acid in acetic anhydride, the conditions used for the nitration of 2-acetothiophene [2, 3] and 2-acetofuran [4]. When the reaction was run under the customary conditions for the nitration of alkyl aromatic ketones (acetophenone, etc.) [5], i.e., by treatment with a mixture of concd. nitric and sulfuric acids, we obtained, in addition to the desired mixture of 4-nitro- and 5-nitro-2-acetoselenophenes, also quite a substantial amount of 2,4-dinitroselenophene (from 16 to 21%, based on taken 2-acetoselenophene, and from 22 to 25.5%, based on reacted 2-acetoselenophene). We will mention that when we nitrated 2-selenophenecarboxaldehyde [6] with a mixture of fuming nitric and concd. sulfuric acids, the formation of 2,4-dinitroselenophene occurred to an even greater degree, and its yield reached 38%.

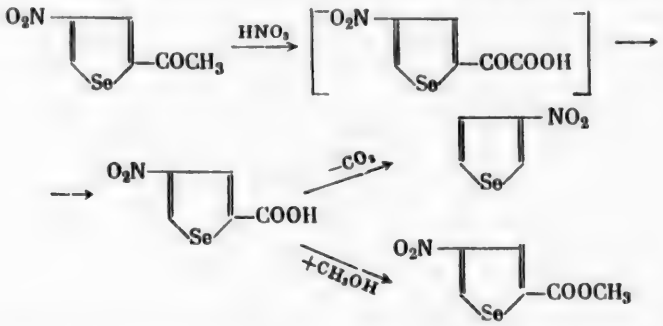
The appearance of 2,4-dinitroselenophene in the nitration product of 2-acetoselenophene is explained by the fact that the nitration mixture causes a partial replacement of the acetyl group by the nitro group with the formation of 2-nitroselenophene, which on further nitration yields 2,4-dinitroselenophene.



It should be mentioned that in the thiophene series [7] such a replacement of the acetyl group by the nitro group has not been observed as yet, possibly because the nitration of 2-acetothiophene was run with fuming nitric acid in acetic anhydride, and not with mixed acid. In the furan series a replacement of the acetyl group by the nitro group was observed by Rinkes [4], who nitrated 1-acetofuran with fuming nitric acid in acetic anhydride and obtained, in addition to 5-nitro-2-acetylfuran (31%), up to 13.5% of 2-nitrofuran.

However, a replacement of the acetyl group by the nitro group during the nitration of 2-acetoselenophene can also occur in the 4-nitro-2-acetoselenophene that is formed. Actually, we obtained up to 8% of 2,4-dinitroselenophene when we treated 4-nitro-2-acetoselenophene with a mixture of concd. nitric and sulfuric acids. This explains the increase in the 2,4-dinitroselenophene yield (from 19 to 21%) and a corresponding decrease in the 4-nitro-2-acetoselenophene yield (from 27 to 23%) when the time of nitrating 2-acetoselenophene is increased from 1.5 to 2.5 hr. The yield of mixed 4-nitro- and 5-nitro-2-acetoselenophenes is 46.5% (based on reacted 2-acetoselenophene) when the reaction is run for the optimum length of time (1.5 hr). To separate the 4-nitro-2-acetoselenophene from the small amount of 5-nitro-2-acetoselenophene it is sufficient to treat the mixture with a small amount of warm ether, and then recrystallize the insoluble portion once from alcohol.

When 4-nitro-2-acetoselenophene was oxidized with dilute nitric acid we obtained a mixture of 4-nitro-2-selenophenecarboxylic acid and 4-nitro-2-selenopheneglyoxylic acid, which on further oxidation with hydrogen peroxide gave 4-nitro-2-selenophenecarboxylic acid. We obtained the methyl ester when 4-nitro-2-selenophenecarboxylic acid was esterified, while decarboxylation of the acid gave 3-nitroselenophene.



As regards the 5-nitro-2-acetoselenophene formed along with the other nitration products of 2-acetoselenophene, we were unable to isolate it from the reaction mixture. We established its presence and amount on the basis of the data obtained in studying the ultraviolet absorption spectra of the obtained mixture of semicarbazones.

The absorption spectra of 4-nitro- and 5-nitro-2-acetoselenophene are shown in Fig. 1.

To determine the amount of 4-nitro- and 5-nitro-2-acetoselenophene in the nitration product of 2-acetoselenophene, we took the following spectra: a) the semicarbazone of each of these nitro ketones, and b) the spectrum of the crude mixture of semicarbazones obtained by reacting semicarbazide with the nitration product obtained after removal of the 2,4-dinitroselenophene from it, with subsequent sublimation (to remove tarry impurities). A comparison of the curves of the absorption spectra of the crude mixture of nitro-ketone semicarbazones with those of the semicarbazone standards of each of these nitro ketones, given in Fig. 2, reveals that the indicated mixture contains 85% of 4-nitro-2-acetoselenophene semicarbazone and 15% of 5-nitro-2-acetoselenophene semicarbazone; the absorption curve of this mixture coincides with the curve of the artificially prepared mixture of semicarbazones of the same composition.

It should be mentioned that when we nitrated 2-selenophenecarboxaldehyde with fuming nitric acid in concd. sulfuric acid, we also obtained a mixture of isomeric nitroaldehydes, containing 90% of 4-nitro-2-selenophenecarboxaldehyde and 10% of 5-nitro-2-selenophenecarboxaldehyde [6].

As a result, if a meta-orienting group, for example, - NO_2, -COOH, -CHO, -$COCH_3$, is found in the α-position of the selenophene ring, then when such a compound in the selenophene series is nitrated, the nitro group enters into the β-position of the ring, in which connection the simultaneous entrance of the nitro group into the α'-position occurs only as a side reaction. Consequently, in this case the influence of the m-orienting substituent is considerably greater than the influence of the heteroatom—selenium, which directs the entering substituent into the α-position of the ring.

It is interesting to mention that the nitration of furan derivatives containing a m-orienting substituent in the 2-position of the ring yields only 5-nitro derivatives, while the nitration of the corresponding thiophene derivatives yields a mixture of 4- and 5-nitro derivatives. Thus, the nitration of 2-nitrothiophene [8] with

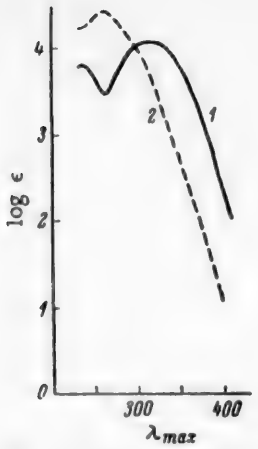


Fig. 1. Ultraviolet absorption spectra. 1) 5-Nitro-2-acetoselenophene; 2) 4-nitro-2-acetoselenophene.

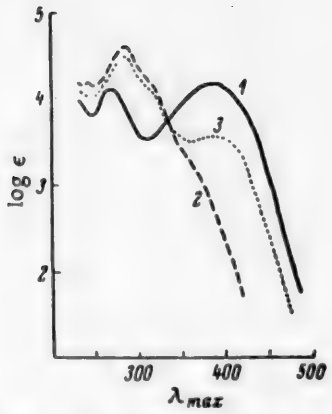


Fig. 2. Ultraviolet absorption spectra. 1) 5-Nitro-2-acetoselenophene semicarbazone; 2) 4-nitro-2-acetoselenophene semicarbazone; 3) crude mixture of semicarbazones, obtained from the mixture of isomeric nitro-ketones isolated from the nitration product of 2-acetoselenophene.

mixed acid yields a mixture containing 85% 2,4-dinitrothiophene and 15% 2,5-dinitrothiophene; the nitration of 2-acetothiophene (with fuming nitric acid in acetic anhydride) [3] and of 2-thiophenecarboxaldehyde (with mixed acid) [9] yields in both cases a mixture containing approximately equal amounts of the 4- and 5-nitro derivatives. The nitration of benzaldehyde and of acetophenone with mixed acid gives exclusively the m-derivatives.

Consequently, the influence of the heteroatom decreases in the order furan > thiophene > selenophene; this undoubtedly is linked with a decrease in the electronegativity, sharply manifest in going from oxygen to sulfur and selenium (the electronegativity of oxygen is 3.5, of sulfur 2.5, and of selenium 2.4) [10], and the resultant increase in the polarizability of these atoms, as a result of which the influence of a meta-orienting group found in the α-position increases.

A comparison of the results to which such a nonconformance in the orientation leads when 2-acylated derivatives of furan, thiophene and selenophene are nitrated indicates that selenophene lies closer to benzene than does thiophene.

EXPERIMENTAL

4-Nitro-2-acetoselenophene. To 12 ml of concd. sulfuric acid at -5° was slowly added, with stirring, 6.92 g (0.04 mole) of 2-acetoselenophene, and then a nitrating mixture composed of 4.54 g (0.052 mole) of nitric acid (d 1.43) and 4.8 ml of concd. sulfuric acid, cooled to 0°, was added in 30 min at such a rate that the temperature stayed between -5 and -2°. After stirring for 1 hr, the reaction mixture was poured into a mixture of 60 g of ice and 120 ml of water, after which the precipitate was filtered, washed with ice-cold water, and triturated well in a small beaker with two portions of alcohol (5 ml each); the residue (2.02 g) was a mixture of the 4- and 5-nitro-2-acetoselenophenes.

The aqueous filtrates were extracted with ether, the combined extracts washed with 1 N caustic solution, then with water, dried over sodium sulfate, the ether distilled off, and the oily residue triturated with 2 ml of alcohol; the precipitate (0.24 g) was filtered and added to the mixture of isomers.

The alcohol was distilled from the alcohol extracts; vacuum distillation of the residue gave 1.54 g of unchanged ketone (b.p. 95-110° at 5 mm) and 3.04 g of a mixture of isomeric nitro-ketones and 2,4-dinitroselenophene, which distilled at 140-148° (5 mm) and solidified on cooling. This fraction was triturated twice with 5-ml portions of ether; the residue (0.9 g) was a mixture of isomeric nitro-ketones, the total yield of which was 3.16 g (36% based on taken 2-acetoselenophene and 46.5% based on reacted 2-acetoselenophene).

To isolate the 4-nitro-2-acetoselenophene we took the 3.16 g of mixture and heated it with 7 ml of absolute ether, after which the precipitate was filtered and recrystallized from alcohol. We obtained 2.34 g (27% on taken and 34.5% on reacted 2-acetoselenophene) of 4-nitro-2-acetoselenophene as white crystals with m.p. 123-123.5°.

Found %: C 33.35, 33.32; H 2.23, 2.20; Se 36.02, 36.17. $C_6H_5O_3NSe$. Calculated %: C 33.06; H 2.31; Se 36.21.

The nitration of 8.65 g (0.05 mole) of 2-acetoselenophene in 11 g of acetic anhydride with 4.7 g of fuming nitric acid (d 1.50) in 46 g of acetic anhydride at -6 to -10°, with subsequent treatment of the reaction product as described above, gave 1.03 g (9.5%) of mixed 4-nitro- and 5-nitro-2-acetoselenophenes, and we also isolated 3.8 g of unchanged ketone.

2,4-Dinitroselenophene. After distilling off the ether from the ether filtrates (from washing the mixture of nitro-ketones and 2,4-dinitroselenophene) we obtained 1.70 g (19% on taken and 24.5% on reacted 2-acetoselenophene) of 2,4-dinitroselenophene with m.p. 78.5-79° (from petroleum ether). The mixed melting point with authentic 2,4-dinitroselenophene was not depressed. Literature data [6, 11]: m.p. 78-79°.

When the reaction was run for 50 min the yield of 4-nitro-2-acetoselenophene was 2.06 g, and the yield of 2,4-dinitroselenophene was 1.42 g; when the reaction was run for 2.5 hr the yield of nitro-ketone dropped to 1.98 g, and that of 2,4-dinitroselenophene increased to 1.86 g.

Nitration of 4-nitro-2-acetoselenophene. To 6 ml of concd. sulfuric acid at -5° was added 1.09 g (0.005 mole) of 4-nitro-2-acetoselenophene, and then a mixture of 2.27 g (0.026 mole) of nitric acid (d 1.43) and 2.4 ml of concd. sulfuric acid was added in 10 min, after which the reaction mixture was stirred for 1.5 hr, poured into a mixture of 30 g of ice and 60 ml of water, and the product extracted with ether. The ether extracts were washed with water and then dried; the ether was distilled off, and the residue (0.87 g) was dissolved in 15 ml of alcohol and the solution treated with 0.44 g of semicarbazide hydrochloride in 5 ml of water, after which the mixture was refluxed for 10 min, cooled, and diluted with 15 ml of water; the precipitate of 4-nitro-2-acetoselenophene semicarbazonewas filtered and washed with warm ether; the filtrate (after distilling off the alcohol) was extracted with ether and the extracts were combined. Removal of the ether by distillation gave 0.09 g (8%) of 2,4-dinitroselenophene with m.p. 78.5-79° (from petroleum ether); the mixed melting point with authentic 2,4-dinitroselenophene was not depressed.

4-Nitro-2-acetoselenophene semicarbazone. From 0.55 g (0.0025 mole) of the nitro-ketone we obtained 0.63 g (91%) of the semicarbazone as bright yellow crystals with m.p. 243-244° (decompn.) (from alcohol).

Found %: C 30.76, 30.88; H 2.81, 2.95; Se 28.51, 28.71. $C_7H_8O_3N_4Se$. Calculated %: C 30.56; H 2.93; Se 28.69.

Mixed 4-nitro- and 5-nitro-2-acetoselenophene semicarbazones. The vacuum sublimation of 0.6 g of mixed isomeric nitro-ketones (taken from the total amount of 3.16 g) at 140-150° (10 mm) to remove tarry impurities gave 0.55 g of crystals with m.p. 108-114°, which when reacted with semicarbazide gave 0.6 g (86.5%) of mixed semicarbazones; m.p. 232-233° (decompn.).

Found %: Se 28.40, 28.49. $C_7H_8O_3N_4Se$. Calculated %: Se 28.69.

4-Nitro-2-selenophenecarboxylic acid. To 2.18 g of 4-nitro-2-acetoselenophene in 24 ml of boiling water was gradually added 20 ml of dilute nitric acid (d 1.16), after which the mixture was refluxed for 8 hr, filtered, cooled, and extracted with ether. The ether extracts were treated with sodium bicarbonate solution, and the aqueous solution was separated, acidified with hydrochloric acid, and extracted with ether. The ether was distilled off, the residue was treated with 2 ml of water and 1 ml of 40% hydrogen peroxide, and the mixture was then refluxed for 10 min and cooled. We obtained 0.8 g (36%) of white crystals with m.p. 170-171° (from water).

Found %: C 27.08, 27.16; H 1.64, 1.49; Se 35.82, 35.97. $C_5H_3O_4NSe$. Calculated %: C 27.29; H 1.37; Se 35.89.

Methyl ester of 4-nitro-2-selenophenecarboxylic acid. A solution of 0.44 g of 4-nitro-2-selenophenecarboxylic acid in 8 ml of anhydrous methanol was saturated with dry hydrogen chloride under cooling and then allowed to stand for 18 hr. The mixture was then poured into 30 ml of water, made alkaline with sodium bicarbonate, and the precipitate filtered. We obtained 0.45 g (78%) of white crystals with m.p. 103.5-104° (from petroleum ether).

Found %: C 31.02, 30.88; H 2.31, 2.18; Se 33.55, 33.61. $C_6H_5O_4NSe$. Calculated %: C 30.78; H 2.15; Se 33.76.

3-Nitroselenophene. A mixture of 0.55 g of 4-nitro-2-selenophenecarboxylic acid in 3 ml of quinoline and 0.2 g of freshly reduced copper powder was slowly heated in an oil bath to 215°; vigorous carbon dioxide evolution occurred at 140-160°. To the reaction mixture after cooling was added 15 ml of dilute (1 : 1) hydrochloric acid and the 3-nitroselenophene was steam distilled. We obtained 0.22 g (50%) of compound with m.p. 77.5-78° (from petroleum ether). The mixed melting point with authentic 3-nitroselenophene was not depressed. Literature data: m.p. 77.5-78° [6]; 77-78.5° [11].

The ultraviolet absorption spectra of 4-nitro- and 5-nitro-2-acetoselenophene and their semicarbazones were taken using an SF-4 spectrometer with manual recording (in quartz cuvettes using a hydrogen lamp); methanol was used as the solvent. The data, obtained as a result of the measurements, are given in the table.

Name of compound	Concentration, (M)	Absorption maxima	
		mμ	εα
4-Nitro-2-acetoselenophene	10^{-5}	232	16980
	10^{-5}	260	26300
5-Nitro-2-acetoselenophene	10^{-4}	262	2754
	10^{-5}	315	12300
4-Nitro-2-acetoselenophene semicarbazone	10^{-5}	285	37150
5-Nitro-2-acetoselenophene semicarbazone	10^{-5}	267	12880
	10^{-5}	387	13490
Crude mixture of semicarbazones, obtained from the mixture of isomeric nitro-ketones isolated from the nitration product of 2-acetoselenophene	10^{-5}	284	29510
	10^{-4}	390	3311
Artificial mixture of the semicarbazones of 4-nitro-2-acetoselenophene (85%) and 5-nitro-2-acetoselenophene (15%)	10^{-5}	285	27950
	10^{-4}	389	3452

SUMMARY

1. The reaction product from the nitration of 2-acetoselenophene with mixed acid is a mixture of 4-nitro-2-acetoselenophene (50%), 5-nitro-2-acetoselenophene (8.5%), and 2,4-dinitroselenophene (41.5%).

2. The oxidation of 4-nitro-2-acetoselenophene with dilute nitric acid yields 4-nitro-2-selenophenecarboxylic acid, while its decarboxylation yields 3-nitroselenophene.

3. The ultraviolet absorption spectra of 4-nitro- and 5-nitro-2-acetoselenophene, and also of their semicarbazones, were used to establish the composition of the mixture of nitro-ketones.

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δ-LACTONES

XX.• CLEAVAGE OF HYDROGEN BROMIDE FROM ESTERS OF ACYCLIC γ-BROMO-δ-OXO ACIDS

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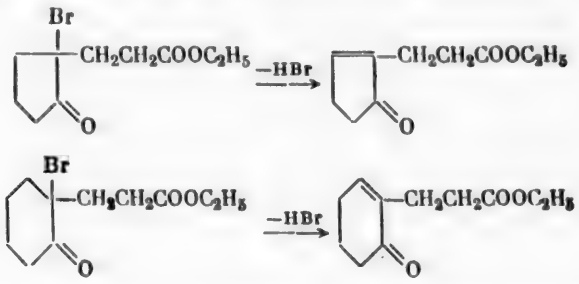
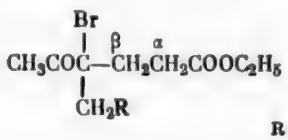
γ-Bromo-δ-oxo acids and their esters (compounds that have remained almost unknown in the literature until recently) have become readily available as the result of the method developed by us earlier for their synthesis, consisting of the reaction of the dibromides of δ-enol lactones with water or alcohols [1]. A study of the reactivity of these compounds is of interest both for synthetic purposes and in order to develop concepts regarding the ring-chain tautomerism of δ-oxo acids.

We had shown earlier that γ-bromo-δ-oxo acids, cleaving hydrogen bromide, form butyrolactones, acylated in the 5 position [2]. The cleavage of hydrogen bromide from esters of γ-bromo-δ-oxo acids was investigated earlier on the example of the esters of cyclic bromo-oxo acids. It proved that 2-bromo-2-(β-carbethoxyethyl)-cyclopentanone and 2-bromo-2-(β-carbethoxyethyl)cyclohexanone easily cleave hydrogen bromide even on distillation, being converted to the esters of the corresponding unsaturated oxo acids; it was shown that the double bond in these esters is found in the ring, and not in the semicyclic position [3].



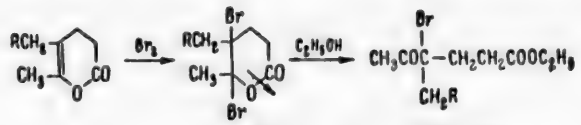
In the present paper our objective was to determine in which of the two possible directions the cleavage of hydrogen bromide takes place from the esters of acyclic γ-bromo-δ-oxo acids of general formula



R = C_2H_5 and C_3H_7.

•For Communication XIX see: Doklady Akad. Nauk SSSR 126, 589 (1959). [See C. B. translation, p. 385.]

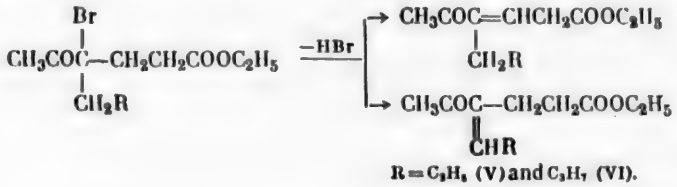
The starting ethyl esters of the acyclic γ-bromo- δ- acids (γ-bromo-γ-acetylenanthic and γ-bromo-γ-acetylcaprylic) were obtained by reacting ethyl alcohol with the dibromides of the corresponding δ-enol lactones.



(I, II) (III, IV)

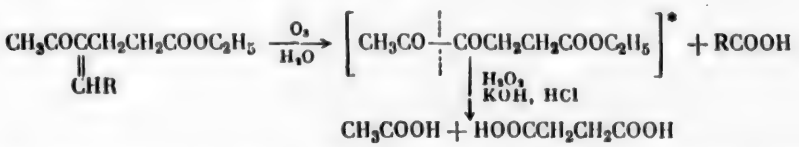
R = C_5H_9 (I, III); C_3H_7 (II, IV).

In contrast to the esters of the acyclic γ-bromo-δ-oxo acids studied by us earlier [1], the bromo esters (III and IV) obtained in the present study partially cleaved hydrogen bromide even when vacuum distilled and consequently could not be obtained analytically pure. Complete cleavage of hydrogen bromide from the synthesized bromo esters was accomplished by heating them with diethylaniline; here we obtained the esters of the unsaturated oxo acids (V and VI) in 77-97% yields. The cleavage of hydrogen bromide could have gone in two directions:



R = C_5H_9 (V) and C_3H_7 (VI).

Ozonolysis of the obtained unsaturated esters (V and VI) revealed that the hydrogen bromide cleavage goes only along the second direction. In both cases succinic acid was isolated from the hydrolysis products of the ozonides, which could have been formed only if the double bond in the starting unsaturated esters was found in the γ, δ-position with respect to the carbethoxyl group.



Malonic acid, the formation of which could be expected if the hydrogen bromide cleavage had gone in the first direction, was not found in the hydrolysis product of the ozonides.

In this manner, by the cleavage of hydrogen bromide from the esters of acyclic γ-bromo- δ-oxo acids, we obtained the previously unknown esters of 4-acetyl-4-alkenoic acids, which at the same time are β-carbethoxyethyl derivatives of methyl vinyl ketones.

The results obtained in the present study permit the conclusion that in esters of acyclic γ-bromo- δ-oxo acids the hydrogen atom found in the β-position with respect to the carbonyl and carbethoxyl groups is immobile and does not take part in the formation of hydrogen bromide.

EXPERIMENTAL

5,6-Dibromo-5,6-dialkyl- δ-enollactones (I and II). The starting δ-lactones, 6-methyl-5-propyl-δ-enollactone (b.p. 84-85° at 3 mm, $n^{20}D$ 1.4684, d^{20}_4 1.0054) and 6-methyl-5-butyl-δ-enollactone (b.p. 87-88° at 3 mm, $n^{20}D$ 1.4673, d^{20}_4 0.9894), were obtained by the procedure described by us earlier [5]. To a solution of 0.24 mole of the lactone in 25 ml of absolute ether, with ice-salt cooling and constant shaking, was added 0.24 mole of bromine in drops. The ether was evaporated in vacuo in a stream of dry air. The dibromides (I and II) were obtained as oils that fumed strongly in the air.

•Cleavage of the carbon bond between the carbonyl groups of α-diketones when oxidized with hydrogen peroxide is reported in the literature [4].

Ethyl esters of γ-bromo-δ-oxo acids (III and IV). A 5-fold excess of anhydrous alcohol was added in the cold and with stirring to the above dibromides (I and II) (immediately after their preparation); here the dibromides dissolved in the alcohol with much heat evolution. After 30-40 min the mixture was poured into 50 ml of cold water, the bromo ester layer was separated, and the aqueous alcohol solution was extracted with ether. The ether solution was then dried, the ether evaporated, and the residue vacuum distilled.

Ethyl esters of γ-bromo-γ-acetylenanthic acid (III) (4-bromo-4-propyl-5-oxohexanoic acid) and γ-bromo-γ-acetylcaprylic acid (IV) (4-bromo-4-butyl-5-oxohexanoic acid). These esters were not isolated in the pure state, since on distillation they partially cleaved hydrogen bromide. For reaction with diethylaniline we used the fraction with b.p. 110-123° (3 mm) and $n^{20}D$ 1.4628, and with b.p. 145-160° (13 mm) and $n^{20}D$ 1.4760, respectively, obtained after one distillation of the products obtained from the reaction of dibromolactones (I and II) with alcohol, and being bromo esters (III and IV) with the unsaturated esters (V and VI) present as impurity.

Ethyl esters of unsaturated δ-oxo acids (V and VI). A mixture of 0.1 mole of the bromo ester and 0.1 mole of diethylaniline was heated on the water bath for 3 hr. The reaction mass, which crystallized on cooling, was treated with 4 ml of dilute (1 : 1) hydrochloric acid and the whole was then extracted 10-15 times with benzene. The benzene solution was dried over fused magnesium sulfate, the solvent distilled off, and the residue was first vacuum distilled, and then fractionated through a column (20 theoretical plates). An attempt to obtain (in conventional manner) the semicarbazones, and also the 2,4-dinitrophenylhydrazones of the unsaturated esters (V and VI) proved unsuccessful.

The ethyl ester of 4-acetyl-4-heptenoic acid (V) was obtained in 77% yield.

B.p. 127-127.5° at 11 mm, 107-108° at 5 mm, $n^{20}D$ 1.4556, d^{20}_4 0.9942, MR_D 54.24. $C_{11}H_{18}O_3F$. Calculated: 64.19.

Found %: C 66.23, 66.33; H 9.18, 9.27. $C_{11}H_{18}O_3$. Calculated %: C 66.60; H 9.09.

The ethyl ester of 4-acetyl-4-octenoic acid (VI) was obtained in 97% yield.

B.p. 130° at 4 mm, 108-109° at 3 mm, $n^{20}D$ 1.4595, d^{20}_4 0.9886, MR_D 58.73. $C_{12}H_{20}O_3F$. Calculated 58.81.

Found %: C 68.12, 68.13; H 9.42, 9.32. $C_{12}H_{20}O_3$. Calculated %: C 67.87; H 9.46.

Ozonolysis of unsaturated esters (V and VI). A stream of oxygen containing 4% ozone was passed at a rate of 5 liters per hour into a solution of 7 g of the unsaturated ester in 20 ml of carbon tetrachloride for 4-5 hr (with ice cooling). Then 80 ml of water was added to the reaction mixture and the whole allowed to stand overnight. The next day the mixture was heated cautiously for 4 hr then 10 ml of 30% hydrogen peroxide was added and the mixture refluxed for another 4 hr. The solution was made alkaline, the carbon tetrachloride• was steam distilled, and the residual solution was evaporated to dryness on the water bath. The residue was treated with 10 ml of concd. hydrochloric acid, and the mixture was extracted 5-6 times with ether. The ether solution was dried, the solvent was distilled off, and the residue was distilled.

a) Distillation of the decomposition products of the ozonide from the ethyl ester of 4-acetyl-4-heptenoic acid (V) gave: acetic acid with b.p. 116-120° and $n^{20}D$ 1.3702 (literature data [6]: b.p. 118.7°, $n^{20}D$ 1.3698), propionic acid with b.p. 139-140° and $n^{20}D$ 1.3880 (literature data: b. p. 140.9° [7], $n^{20}D$ 1.3865 [8]), and succinic acid with m.p. 180-182° (from water); (literature data: m.p. 181° [9], 185° [10]); the mixed melting point with authentic succinic acid was not depressed.

b) Distillation of the decomposition products of the ozonide from the ethyl ester of 4-acetyl-4-octenoic acid (VI) gave: acetic acid with b.p. 115-120° and $n^{20}D$ 1.3652 (also identified as the acetanilide with m.p. 110-111°), butyric acid with b.p. 155-160° and $n^{20}D$ 1.3995; anilide, m.p. 90° (literature data: b.p. 161.5-162.5°[11], $n^{20}D$ 1.3975 [12], melting point of anilide 92° [13]), and succinic acid, m.p. 180-181° (from water).

SUMMARY

1. It was shown that the cleavage of hydrogen bromide from acyclic esters of γ-bromo-δ-oxo acids in the presence of diethylaniline goes along one of two possible directions and leads to obtaining the esters of 4-acetyl-4-alkenoic acids.

•In both cases a second slow distillation of the carbon tetrachloride failed to reveal the presence of any neutral ozonolysis products (ketones).

2. In this manner we obtained the previously unknown ethyl esters of 4-acetyl-4-heptenoic acid and 4-acetyl-4-octenoic acid in yields of 77 and 97%, respectively.

3. It was established that in esters of γ-bromo-δ-oxo acids the hydrogen atom found in the β-position with respect to the carbonyl and carbethoxyl groups is immobile and does not take part in the formation of hydrogen bromide when the latter is cleaved.

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CYCLOPROPANES AND CYCLOBUTANES

X.• THE ACYLATION OF CYCLOPROPANE HYDROCARBONS

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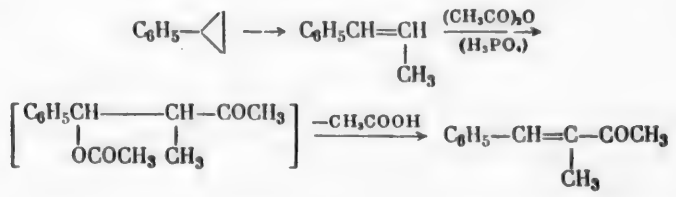
In our previous papers we established that in many reactions the behavior of the cyclopropane hydrocarbons resembles that of the ethylenic hydrocarbons. Thus, the three-membered ring of alkyl- and arylcyclopropanes is opened when these compounds are reacted with mercury acetate in either aqueous or alcoholic solution [1]; the arylcyclopropanes alkylate (propylate) benzene and its derivatives, forming 1,1-diarylpropanes [2].

In this paper we studied the behavior of the three-membered ring in phenylcyclopropane when the latter is acylated with acetic anhydride in the presence of a catalyst, i.e., in the Kondakov reaction, characteristic for hydrocarbons of the ethylene series.•• Phosphoric acid was used as the catalyst (it had been used earlier as a catalyst in the acylation of acyclic compounds [5] and five-membered heterocycles [6]). Previously it had been established on the example of cumene that the benzene ring fails to acylate in the presence of this catalyst (under the conditions used by us), whereas the reaction could be expected to go if aluminum chloride is used as the catalyst.

The acylation of phenylcyclopropane at 20° with acetic anhydride in the presence of phosphoric acid led to the formation of an unsaturated ketone in low yield. By studying the ultraviolet absorption spectrum of the 2,4-dinitrophenylhydrazone of this ketone, it was established that the double bond in it is found in the α, β-position to the CO group. A study of the Raman spectrum of the unreacted hydrocarbon fraction (about 90%) revealed that this fraction contains, besides unchanged phenylcyclopropane, also some propenylbenzene. These two facts caused us to conclude that the phenylcyclopropane is first isomerized to propenylbenzene, and then this compound is the one that acylates.



To confirm such a mechanism for the acylation of phenylcyclopropane in the acylation reaction (under the same conditions) we added propenylbenzene to the reaction mixture; here we obtained (in much higher yield)

•For Communication IX see: Doklady Akad. Nauk SSSR 127, 111 (1959).[See C. B. translation, p. 509.]

•• Papers [3, 4] exist in the literature in which the acylation of cyclopropane is described; it was shown that the products of this reaction are β-chloro ketones, and they can be converted to α, β-unsaturated ketones.

an unsaturated ketone that proved to be identical with the ketone obtained from phenylcyclopropane (from the melting point, ultraviolet absorption spectrum,• and melting point of the 2,4-dinitrophenylhydrazone).

$$C_6H_5CH{=}CHCH_3 + (CH_3CO)_2O \xrightarrow{H_3PO_4} C_6H_5CH{=}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}{-}COCH_3$$

The structure of the obtained 2-benzylidenebutanone was proved conclusively by its counter synthesis, which consisted of the crotonic condensation of methyl ethyl ketone (at the methylene group) with benzaldehyde in the presence of hydrogen chloride [7].

$$C_6H_5CHO + \underset{\displaystyle CH_3}{\overset{\displaystyle |}{CH_2}}{-}COCH_3 \xrightarrow{(HCl)} C_6H_5CH{=}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}{-}COCH_3$$

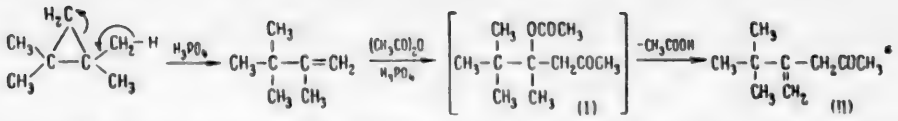
The mixed melting points of the three different preparations of unsaturated ketone, and likewise of their 2,4-dinitrophenylhydrazones, were not depressed. The ultraviolet absorption spectra of the 2,4-dinitrophenylhydrazones of the ketones obtained from either phenylcyclopropane or propenylbenzene, and also by counter synthesis, showed an absorption maximum at 363 mμ, which indicated the presence of conjugation between the C = C and C = O double bonds [8].

Since the intermediate stage when phenylcyclopropane was acylated in the presence of phosphoric acid was its isomerization to propenylbenzene, we studied this reaction in greater detail. It was established by the Raman spectrum method that the isomerization of phenylcyclopropane at 20° goes to very slight degree (1-3%) if pure phosphoric acid or its 20% solution in acetic anhydride is used (in accordance with this, a low yield of unsaturated ketone was obtained when phenylcyclopropane was acylated under these conditions).

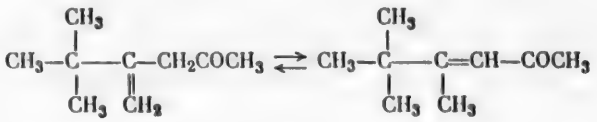
The behavior of cyclopropane hydrocarbons in the acylation reaction (under the above conditions) was investigated by us further on the example of one of the alkylcyclopropanes, namely 1,1,2,2-tetramethylcyclopropane. It was established that the acylation of the latter with acetic anhydride in the presence of phosphoric acid yields an unsaturated ketone in which the double bond is not found in conjugation with the carbonyl group (based on the ultraviolet absorption spectra of both the ketone and its 2,4-dinitrophenylhydrazone). Judging from the Raman spectrum, the hydrocarbon that failed to acylate contained about 10% of unchanged tetramethylcyclopropane, about 10% of 2,4-dimethyl-2-pentene, and about 80% of 2,2,3-trimethylbutene (triptene). By means of individual experiments it was shown that the tetramethylcyclopropane, under the influence of phosphoric acid, isomerizes (at 20°) to triptene to the extent of about 10%, while under the influence of a 20% solution of phosphoric acid in acetic anhydride it isomerizes to triptene to the extent of about 30%. If it is considered that when the tetramethylcyclopropane is acylated (i.e., under the influence of a much more dilute solution of phosphoric acid in acetic anhydride) it isomerizes to triptene to the extent of about 80%, then it is possible to conclude that the tetramethylcyclopropane is isomerized (with an opening of the three-membered ring) with much greater ease than is phenylcyclopropane, and the extent of isomerization is greater the more dilute the solution of phosphoric acid in acetic anhydride used as the isomerization and acylation catalyst.

The acylation of triptene with acetic anhydride in the presence of phosphoric acid led to the formation of an unsaturated ketone that proved to be identical in all of its properties with the ketone obtained from the tetramethylcyclopropane; the mixed melting point of the 2,4-dinitrophenylhydrazones of the two ketone preparations was not depressed. The hydrocarbon fraction recovered from the acylation of triptene was wholly unchanged triptene (the isomeric 2,4-dimethyl-2-pentene was not present). Consequently, the isomerization of the tetramethylcyclopropane under the influence of phosphoric acid goes mainly with the formation of triptene (which is found in agreement with the heterolytic character of the isomerization of cyclopropanes under the influence of acids), which then enters into the acylation reaction; since the unsaturated ketone formed here did not have the double bond in the α,β-position to the carbonyl group (the 2,4-dinitrophenylhydrazone shows maximum absorption at 324 mμ [8]), then obviously the reaction went in the following manner.

• The ultraviolet absorption spectra were taken in the Molecular Spectroscopy Laboratory of the Department of Organic Chemistry, for which we wish to thank L. A. Kazitsina.

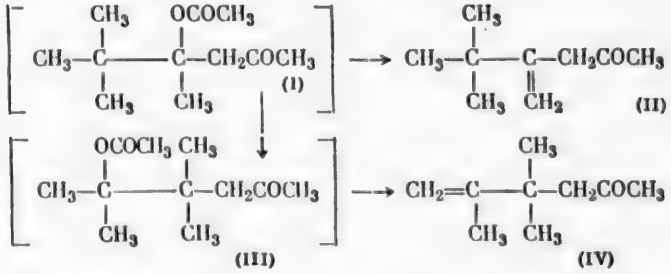


It proved further that the obtained β,γ-unsaturated ketone (2,2-dimethyl-3-methylene-5-hexanone) isomerized partially (by about 50%) on long standing, forming an equilibrium mixture of two ketones—the starting ketone and its isomer with the double bond in the α,β-position (the 2,4-dinitrophenylhydrazone of the mixed ketones showed maximum absorption at 351 mμ).



The same equilibrium mixture of the α,β- and β,γ-forms of the unsaturated ketone was obtained when the starting β,γ-form was refluxed with 20% sulfuric acid for 1 hour. The composition of the obtained mixture of ketones failed to change when the mixture was refluxed for a longer time (5 hr) with sulfuric acid.

An examination of the scheme given above for the acylation of the tetramethylcyclopropane and triptene leads to the thought that it might be possible to form the β,γ-unsaturated ketone not only by the direct cleavage of acetic acid (II), but also by its cleavage (IV) after prior retropinacoline rearrangement (III) of the intermediately formed oxoacetate (I).



Ketones (II) and (IV) have a different carbon skeleton. However, it was established that the obtained β,γ-unsaturated ketone, isomerizing (when allowed to stand) with a shift of the double bond toward the carbonyl group, retains its carbon skeleton: Hydrogenation in the cold of the starting ketone (pure β,γ-form), and of its mixture with the α,β-form, led to the formation of saturated ketones, which proved to be identical in all of their properties. Since the α,β-form can be formed without change in the carbon skeleton only from ketone (II), it is obvious that obtaining the β,γ-unsaturated ketone from oxoacetate (I) went without retropinacoline rearrangement.

EXPERIMENTAL

Acylation of cyclopropanes and of their isomeric alkenes with acetic anhydride in the presence of phosphoric acid. The reaction of acetic anhydride in the presence of phosphoric acid with phenylcyclopropane and propenylbenzene, and also with 1,1,2,2-tetramethylcyclopropane and triptene (2,2,3-trimethylbutene), was run under constant conditions. The reaction mixture, composed of hydrocarbon, acetic anhydride (mole ratio 1:2), and catalyst (being a 20% solution of phosphoric acid in acetic anhydride, prepared the day before reaction), was stirred at 20° for 25-30 hr, and then was poured on ice; the upper layer was washed with 5% sodium carbonate solution and then with water until neutral, after which it was dried over magnesium sulfate and the low-boiling hydrocarbon fraction removed by distillation; the obtained unsaturated ketone was isolated from the residue

• The formation of β,γ-unsaturated ketones when alkenes are acylated by the Kondakov procedure is described in the literature [9].

by vacuum distillation (the yield of ketone was calculated both on the taken and on the reacted hydrocarbon) and was purified by conversion to the semicarbazone, which was recrystallized from alcohol and then decomposed by distillation with aqueous oxalic acid solution.

Acylation of phenylcyclopropane. For reaction we took 100 g of phenylcyclopropane (b.p. 173° at 754 mm, $n^{20}D$ 1.5340 d^{20}_4 0.9440 [10]), 175 g of acetic anhydride, and 10 g of catalyst. The hydrocarbon fraction (90 g, 90% of the phenylcyclopropane taken for reaction) distilled from the reaction product had b.p. 173° (750 mm) and $n^{20}D$ 1.5350. The Raman spectrum of this fraction is given below (the intensities of the lines were determined visually using an arbitrary scale, where the intensity of the line at 1364 cm^{-1} was taken equal to 10):

227 (0.5),307 (0.5; broad), 380 (3, broad), 435 (0), 530 (1), 558 (0.5), 621 (5), 670 (0.5), 735 (7), 769 (0.5) 792 (0.5),813 (2.5), 838 (0.5), 875 (2.5), 900 (5), 942 (2), 963 (0.5), 1000 (30), 1022 (5), 1046 (0.5), 1080 (0.5), 1130 (1), 1160 (3), 1182 (3), 1219 (18), 1240 (0.5), 1270 (1), 1298 (1.5), 1316 (1), 1329 (0.5), 1364 (10), 1427 (1), 1442 (1), 1464 (3), 1493 (1.5), 1546 (1.5), 1580 (1), 1608 (30), 1628 (0.3), 1640 (1), 1664 (2).

A study of the Raman spectrum revealed that this fraction contained about 97% of the starting phenylcyclopropane [10] [frequencies: 1000 (30), 1219 (18), 1364 (10), 1608 (30)], 2-3% of propenylbenzene [frequencies: 1640 (1), 1664 (2)], and traces of α-methylstyrene [frequency: 1628 (0.3)].

The obtained acylation product, the α,β-unsaturated ketone [2-benzylidenebutanone; yield 5 g (4%, or 36.5% based on reacted hydrocarbon)] had the following constants:

B.p. 150° (30 mm), 75° (5 mm); m.p. 36° (from ether).

Found %: C 82.64, 82.68; H 7.63, 7.70. $C_{11}H_{12}O$. Calculated %: C 82.52; H 7.56.

Semicarbazone: m.p. 215° (from alcohol; in a sealed capillary).

Found %: N 19.38, 19.27. $C_{12}H_{15}ON_3$. Calculated %: N 19.35.

2,4-Dinitrophenylhydrazone (red crystals): m.p. 187° (from alcohol).

Ultraviolet absorption spectrum (in isooctane solution): λ_{max} 363 mμ.

Found %: N 16.14, 16.07. $C_{17}H_{16}O_4N_4$. Calculated %: N 16.55.

Acylation of propenylbenzene. For reaction we took 150 g of propenylbenzene (b.p. 175° at 745 mm, $n^{20}D$ 1.5442, d^{20}_4 0.9232 [11]), 260 g of acetic anhydride, and 10 g of catalyst. We recovered 55 g of propenylbenzene (36.7%) from the reaction. The obtained unsaturated ketone [yield 62 g (31.4%, 48% based on reacted hydrocarbon)] distilled at 75° (5 mm) and had m.p. 36° (from ether); 2,4-dinitrophenylhydrazone: m.p. 189° (from alcohol); the ultraviolet absorption spectrum of the compound proved to be identical with the absorption spectrum of the ketone obtained from phenylcyclopropane (λ_{max} 363 mμ, in isooctane). The mixed melting point of the 2,4-dinitrophenylhydrazones obtained from the two ketone preparations (obtained by the acylation of phenylcyclopropane and of propenylbenzene) was not depressed (m.p. 189°).

Counter synthesis of 2-benzylidenebutanone. A stream of dry hydrogen chloride was passed into a mixture of 45 g of methyl ethyl ketone and 62 g of benzaldehyde until saturated. The reaction mixture was washed with 5% NaOH solution and then poured into water. The obtained unsaturated ketone was extracted with ether. The ether extracts were dried over magnesium sulfate, the ether was evaporated, and the ketone crystallized as needles.

M.p. 37° (from alcohol; literature data [7]: m.p. 38°; 2,4-dinitrophenylhydrazone (orange-red crystals): m.p. 190° (from a mixture of alcohol and ethyl acetate).

Isomerization of phenylcyclopropane. A mixture of phenylcyclopropane (15 g) and catalyst (1 g of 20% phosphoric acid in acetic anhydride, or 1 g of pure phosphoric acid) was stirred at 20° for 30 hr. After working up the reaction mixture in the usual manner and distillation, we collected in both cases the hydrocarbon fraction with b.p. 173° (750 mm) and $n^{20}D$ 1.5350, judging from the Raman spectrum, composed of about 97% of phenylcyclopropane [frequencies: 1000 (30), 1219 (18), 1364 (10), 1608 (30)], 2-3% of propenylbenzene (frequencies: 1640 (1), 1664 (2)], and traces of α-methylstyrene [frequency: 1628 (0.3)].

Acylation of 1,1,2,2-tetramethylcyclopropane. From the reaction mixture, composed of 100 g of the tetramethylcyclopropane (b.p. 75° at 754 mm, $n^{20}D$ 1.4010, d^{20}_4 0.7183 [12]), 210 g of acetic anhydride, and 10 g of catalyst, we isolated 80 g of the hydrocarbon fraction (80% of the starting hydrocarbon) with b.p. 76-78 at 745 mm and $n^{20}D$ 1.4020, and 15 g of higher boiling unsaturated ketone with b.p. 162° at 745 mm (yield 10.6%; 53.5% based on reacted hydrocarbon). The distilled hydrocarbon fraction was analyzed spectroscopically:

257 (0.5, broad), 308 (0.5), 353 (1), 390 (1, broad), 460 (0.5), 476 (0.5), 518 (0), 621 (1), 661 (1.5), 675 (35), 687 (1), 808 (1.5, doublet), 843 (1), 860 (2), 897 (2, broad), 925 (3), 950 (4), 996 (0.5), 1038 (1.5), 1105 (1.5), 1144 (1), 1204 (10, broad), 1296 (1.5), 1323 (0.5), 1350 (1), 1382 (4), 1408 (2), 1444 (10), 1463 (10), 1640 (16), 1672 (2.5).

Judging by the given Raman spectrum, the hydrocarbon distillate from the acylation of the tetramethylcyclopropane contained about 80% of triptene (2,2,3-trimethylbutene) [frequency: 1640 (16)], about 10% of 2,4-dimethyl-2-pentene [frequency: 1672 (2.5)], and approximately 10% of unchanged tetramethylcyclopropane [12] [frequencies: 661 (1.5), 860 (2). The isolated ketone had the following constants:

B.p. 162° (745 mm), $n^{20}D$ 1.4530, d^{20}_4 0.8638, MR_D 43.94. $C_9H_{16}OF$. Calculated 43.30.

Found %: C 77.06, 76.86; H 11.41, 11.60. $C_9H_{16}O$. Calculated %: C 77.2; H 11.4.

Semicarbazone: m.p. 205° (in a sealed capillary; after three recrystallizations from alcohol).

Found %: N 20.87, 20.68. $C_{10}H_{19}ON_3$. Calculated %: N 21.30.

2,4-Dinitrophenylhydrazone (yellow crystals): m.p. 140° (from alcohol).

Found %: C 56.09, 56.29; H 6.37, 6.36. $C_{15}H_{20}O_4N_4$. Calculated %: C 56.18; H 6.52.

The ketone and its 2,4-dinitrophenylhydrazone showed ultraviolet absorption maxima at 232 and 342 mμ, respectively, which indicated [8] the absence of conjugation between the C = C and C = O (or C = N) bonds in these compounds and permitted assigning the structure of 2,2-dimethyl-3-methylene-5-cyclohexanone to the obtained ketone.

Isomerization of the tetramethylcyclopropane to triptene. a) A mixture of 1,1,2,2-tetramethylcyclopropane (15 g) and catalyst (1 g of a 20% solution of phosphoric acid in acetic anhydride) was stirred for 30 hr at 20°. After working up the reaction mixture in the usual manner, we isolated the hydrocarbon fraction with b.p. 77° (754 mm) and $n^{20}D$ 1.4017, which was, judging from the spectral analysis data, composed of about 30% triptene [frequency 1640 (7)], traces of 2,4-dimethyl-2-pentene [frequency: 1672 (1)], and about 70% of unchanged tetramethylcyclopropane [12] [frequencies: 661 (10), 860 (7)].

b) A mixture of 15 g of 1,1,2,2-tetramethylcyclopropane and 1 g of phosphoric acid was stirred for 30 hr. The obtained hydrocarbon fraction [b.p. 76° (740 mm), $n^{20}D$ 1.4010] was subjected to spectral analysis. The amount of isomerization product—triptene (with a trace amount of 2,4-dimethyl-2-pentene)—in this case was about 10% [frequency: 1640 (1.5)]; about 90% of the tetramethylcyclopropane was recovered unchanged [frequencies: 661 (30), 860 (20)].

Acylation of triptene (2,2,3-trimethylbutene)—counter synthesis of 2,2-dimethyl-3-methylene-5-hexanone. Triptene (b.p. 78° at 750 mm, $n^{20}D$ 1.4020, d^{20}_4 0.7088) had the following spectrum (visual intensities):

218 (1, broad), 257 (1, broad), 295 (0.5), 355 (7), 390 (2), 462 (2), 490 (2), 556 (1.5), 621 (5), 675 (50), 780 (0.5), 843 (6), 893 (3), 927 (12), 955 (12), 996 (2), 1037 (4), 1107 (3, broad), 1144 (3 broad), 1170 (1 bkg), 1202 (15, broad), 1219 (1.5, bkg), 1296 (2.5), 1323 (2.5), 1384 (12), 1403 (12), 1440 (10), 1456 (9), 1642 (30).

For acylation we took 200 g of triptene, 415 g of acetic anhydride, and 20 g of catalyst. From the reaction products we distilled 161 g (80.5% of the triptene taken for reaction) of hydrocarbon fraction with b.p. 77-78°, having the same constants and Raman spectrum as the starting triptene, and 30 g of the β,γ-unsaturated ketone, 2,2-dimethyl-3-methylene-5-hexanone (yield 10.6%; 54% based on reacted hydrocarbon), with b.p. 162° (750 mm). Semicarbazone: m.p. 205° (from alcohol); 2,4-dinitrophenylhydrazone: m.p. 140° (the ultraviolet absorption spectrum had λ_{max} 342 mμ). The mixed melting points of the semicarbazones and 2,4-dinitrophenylhydrazones from the two ketone preparations (obtained from the tetramethylcyclopropane and from the triptene) were not depressed.

Isomerization of 2,2-dimethyl-3-methylene-5-hexanone to 2,2,3-trimethyl-3-hexen-5-one. a) The standing of 2,2-dimethyl-3-methylene-5-hexanone for six months led to the formation of a mixture of ketones, the 2,4-dinitrophenylhydrazone of which had m.p. 131°. The mixture analyzed about 50% of unchanged 2,2-dimethyl-3-methylene-5-hexanone and about 50% of the isomerization product, the α,β-unsaturated ketone 2,2,3-trimethyl-3-hexen-5-one (the ultraviolet absorption spectrum of the 2,4-dinitrophenylhydrazone from this mixture had a maximum at 351 mμ).

b) 2,2-Dimethyl-3-methylene-5-hexanone (15 g) was refluxed for 1 hr with twice its weight of 20% sulfuric acid solution. The absorption spectrum of the 2,4-dinitrophenylhydrazone from the obtained mixture, after it had been worked up in the usual manner, had the same maximum at 351 mμ. The composition of the mixed ketones did not change when the mixture was refluxed for 2 and for 5 hr with 20% sulfuric acid solution.

Hydrogenation of 2,2-dimethyl-3-methylene-5-hexanone. The hydrogenation was run in the cold using Pt/Pd catalyst. The obtained saturated ketone, 2,2,3-trimethyl-5-hexanone, had the following constants:

B.p. 162° (735 mm), 80° (50 mm), $n^{20}D$ 1.4275, d^{20}_4 0.8350, MR_D 43.82. $C_9H_{18}O$. Calculated 43.77.

Semicarbazone: m.p. 180° (from alcohol; in a sealed capillary).

Found % N 21.35, 21.56. $C_{10}H_{21}ON_3$. Calculated % N 21.1.

2,4-Dinitrophenylhydrazone: m.p. 110° (from alcohol).

Found % N 17.57, 17.65. $C_{15}H_{22}O_4N_4$. Calculated % N 17.4.

The equilibrium mixture of the α,β- and β,γ-forms of the unsaturated ketone, obtained by allowing the pure β,γ-form to stand for six months, was hydrogenated under the same conditions. The saturated ketone had the same constants as those given above, and the mixed melting points of the semicarbazones and 2,4-dinitrophenylhydrazones obtained from the two hydrogenated ketone preparations were not depressed.

SUMMARY

1. The acylation of cyclopropane hydrocarbons with acetic anhydride in the presence of phosphoric acid (as acylation catalyst) at 20° proceeds through the intermediate stage of their isomerization to alkenes, which then suffer acylation, forming unsaturated ketones.

2. Phenylcyclopropane and 1,1,2,2-tetramethylcyclopropane isomerize under the influence of phosphoric acid in acetic anhydride to propenylbenzene and 2,2,3-trimethylbutene (triptene), respectively, which is in agreement with the heterolytic character of the cleavage of a three-membered ring.

3. The acylation of either phenylcyclopropane or propenylbenzene leads to the formation of 2-benzylidenebutanone.

4. The acylation of either 1,1,2,2-tetramethylcyclopropane or triptene yields the β,γ-unsaturated ketone, 2,2-dimethyl-3-methylene-5-hexanone, which is formed from the intermediate reaction product—the acetoxy ketone—by the cleavage of a molecule of acetic acid, in accordance with the mechanism for the pyrolysis of acetates (without retropinacoline rearrangement).

5. The structure of the unsaturated ketones formed in the acylation of phenylcyclopropane and 1,1,2,2-tetramethylcyclopropane was shown by a study of the ultraviolet absorption spectra of their 2,4-dinitrophenylhydrazones, and also by comparing their properties with the properties of the same ketones synthesized by counter routes.

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SYNTHESIS OF DIENES FROM OLEFINS AND ALDEHYDES

I. SYNTHESIS OF ISOPRENE FROM ISOBUTYLENE AND FORMALDEHYDE*

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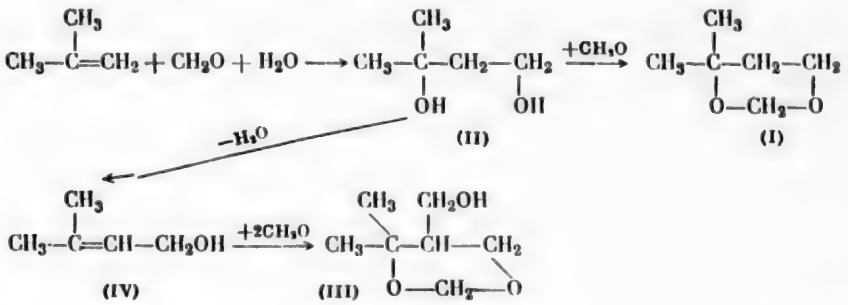
Isoprene is one of the more important dienes used in the synthetic rubber industry. Its importance has grown especially as the result of the discovery of ways to obtain isoprene polymers that have a structure very close to the structure of natural rubber [1]. Of the different isoprene syntheses reported in the literature, only a very few meet the specifications of an industrial process.

For a number of years we have conducted work on the synthesis of isoprene from isobutylene and formaldehyde [2]. In this work it was shown [3, 4] that isobutylene reacts with formaldehyde under mild conditions in the presence of acids (acid concentration 1-1.5%, 85-95°). Here the main reaction product, obtained in 73-76% yield when based on consumed formaldehyde, is 4,4-dimethyl-1,3-dioxane (I), together with some 3-methyl-1,3-butanediol (II) (7-10% yield), the cyclic "dioxane" alcohol 4,4-dimethyl-5-hydroxymethyl-1,3-dioxane (III) (7-8% yield), and a small amount of the unsaturated alcohol (IV) (1-1.5% yield) (Scheme I).



Scheme I

Methods for the synthesis of dienes from alkyldioxanes are disclosed in the patent literature [5]. The scientific literature fails to have a single paper on this subject. In principle it is possible to solve this problem in two ways: a) by the hydrolysis of dimethyldioxane (I) to diol (II) (with subsequent dehydration of the diol to isoprene), in which connection our studies revealed that the hydrolysis of (I) is far from smooth, giving the diol in a yield not exceeding 50% even under the best conditions [6]; and b) by the contact cleavage of (I) to isoprene (with the liberation of formaldehyde and water) in the gas phase over solid catalysts. The last method bears the

*The work was done during 1945-1950.

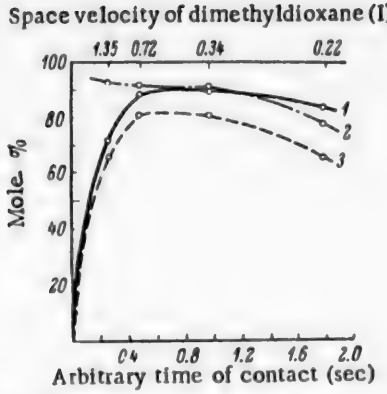


Fig. 1. Contact conversion of dimethyldioxane (I) to isoprene on KSD catalyst at 375° and 1 : 14 (molar) dilution with steam. 1) Conversion of (I) to unsaturated hydrocarbons (C_5H_8 + iso-C_4H_8); 2) isoprene content in unsaturated portion of contact gas; 3) yield of isoprene based on dimethyldioxane passed through.

greatest interest and was worked out by us in very great detail. In addition, it was shown by us that not only dioxane (I), but also the "secondary" products—diol (II) and cyclic alcohol (III)—give isoprene when subjected to contact cleavage.

The selection of a catalyst capable of selectively cleaving the dimethyldioxane to isoprene and having a good activity was made difficult by the fact that analogous reactions are unknown in chemical technology. For this purpose we tested a large number of compounds as catalysts. Some of them, for example aluminum oxide, direct the reaction even at 250° and higher mainly in the direction of cracking to isobutylene and formaldehyde; here the formed formaldehyde decomposes to carbon monoxide and water. Other compounds (catalysts based on silicates) possess a low selectivity, since, together with isoprene, a substantial amount of isobutylene is formed as the result of cracking. A third class of catalysts (phosphoric acid on carriers, boryl phosphate, mixed calcium ammonium phosphate, etc.), although they direct the reaction in the desired direction, strongly "carbonize" and rapidly lose their activity. (All of the catalysts were tested using a mixture of dioxane (I) and steam). The best results were obtained with the phosphate of the Group II metals, especially the calcium phosphates. After long operation we selected a catalyst (KSD) based on a mixture of calcium phosphates of definite composition; this catalyst is characterized by a high activity and selectivity, a good reproducibility, and an adequate stability. Catalysts of this type require regeneration after 2-4 hr of operation with a mixture of steam and air in order to burn off the deposited "carbon," which reduces the activity. Preliminary experiments revealed that these catalysts suffer a sharp reduction in activity if they are heated in the absence of steam. This apparently is linked with the dehydration of the calcium acid phosphates. Dibasic calcium phosphate, for example, is easily converted to the pyrophosphate in accordance with the reaction $2CaHPO_4 \rightleftharpoons Ca_2P_2O_7 + H_2O$; in this case the conversion is reversible, and the reverse reaction takes place in the presence of steam. These same preliminary experiments also revealed that good yields of isoprene are obtained only if the dimethyldioxane is diluted with steam, which apparently is linked with the mechanism of the reaction (see below).

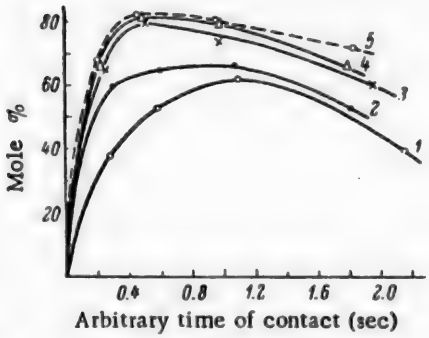


Fig. 2. Conversion of dimethyldioxane (I) to unsaturated hydrocarbons (C_5H_8 + iso-C_4H_8) at different temperatures and a 1 : 14 (molar) dilution with steam. 1) 300°; 2) 325°; 3) 350°; 4) 375°; 5) 400°.

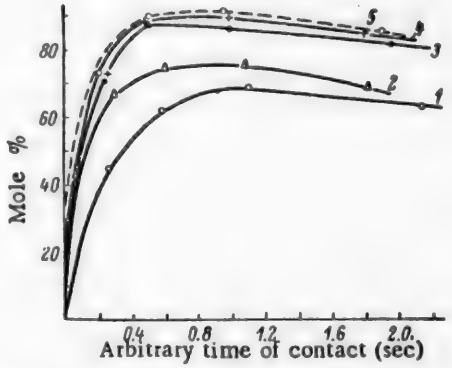


Fig. 3. Yield of isoprene based on dimethyldioxane (I) passed through at different temperatures and a 1 : 14 (molar) dilution with steam. 1) 300°; 2) 325°; 3) 350°; 4) 375°; 5) 400°.

TABLE 1

Effect of Dilution With Steam on the Contact Cleavage of Dimethyldioxane•

Temperature	Space velocity (ml/ml catalyst/hr)		Arbitrary contact time (sec)	Dilution of dimethyldioxane with steam (molar)	Conversion of dimethyldioxane to unsatd. hydrocarbons: isoprene + isobutylene (mol. %)	Amt. of isoprene in unsaturated portion of contact gas (vol. %)	Yield of isoprene based on passed dimethydioxane (mole %)
	dimethyldioxane	water					
302°	0.67	0.67	1.2	6.7	75.6	91.1	69
299	0.67	1.38	0.6	13.4	74.5	88.4	66
299	0.67	2.66	0.32	26.8	76.5	90.2	70
298	0.67	4.00	0.22	40.2	77.9	88.1	70
295	0.67	5.34	0.16	53.6	68.4	91.4	64

•The catalyst resembled KSD, but had a different composition of the components.

Study of the conditions for the contact conversion of dimethyldioxane to isoprene. The character of the conversion of dimethyldioxane on KSD catalyst as a function of the "arbitrary" time of contact (i.e., at different space velocities) and of the temperature is shown in Figs. 1-3. For all of the investigated temperatures the yield of isoprene increases with increase in the contact time only up to a certain limit, after which a decrease sets in, apparently because of secondary reactions (cracking and polymerization). The higher the temperature, the shorter the contact time needed to attain the maximum isoprene yield. If for a temperature of 325° the optimum contact time is 1 sec, then for 375° it is equal to 0.5 sec. The ratio between the other unsaturated hydrocarbons (consisting mainly of isobutylene) and isoprene is practically independent of the extent of dimethyldioxane conversion. Thus, even for a dimethyldioxane conversion as high as 90% this ratio remains practically the same as in the experiments where the degree of conversion is low. With further increase in the extent of conversion beyond 90% the ratio of the unsaturates in the gas increases with a simultaneous decrease in the isoprene yield, which can be explained as due to a cracking of isoprene itself. These facts make it possible to conclude that the secondary reaction of dimethyldioxane cracking to isobutylene and formaldehyde proceeds parallel with the main reaction and independently of it.

Dilution of the dimethyldioxane with steam leads to a substantial acceleration of the reaction (see Table 1). From the data in Table 1 it follows that a 6-fold increase in the rate of adding the water with an approximately like decrease in the contact time failed to affect either the extent of dimethyldioxane conversion or the isoprene yield. From this we arrive at the conclusion that water takes part in the reaction itself. Both of these indices decrease when the amount of added water is increased further, which can be explained as due to a slightly too great reduction in the contact time.

A study of the various factors determining the contact conversion of the dimethyldioxane made it possible to select the optimum conditions for running the reaction, where the yield of isoprene based on passed dimethyldioxane was 75-78%, and 80-85% based on decomposed dimethyldioxane. The continuous contact experiments revealed that both the extent of dimethyldioxane conversion and the isoprene yield decrease with time, for which reason the duration of catalyst operation before regeneration should not exceed 4 hr. The stability of the catalyst under prolonged operating conditions was checked by operating under the optimum conditions in a reactor made of ÉYa-IT steel; here the regeneration of the catalyst was run under predetermined conditions every 2-4 hr. After 450 hr of operation, the catalyst had hardly lost either its activity or its selectivity.

For a more detailed evaluation of the results obtained in the contact experiments we ran material balance experiments, where the best accounting possible was made of all of the reaction products. The material balance was based on the composition and amount of the different gaseous and liquid products collected; here we also took into account the "carbon" deposited on the catalyst. One typical material balance experiment (of a large number) made on the contact decomposition of the alkyldioxane is given in Table 2.

TABLE 2

Material Balance on the Contact Conversion of 4,4-Dimethyldioxane (I) to Isoprene on KSD Catalyst

Process conditions: 375°; space velocity of dimethyldioxane 0.7 ml/ ml catalyst- hr; dilution with steam 1:14 (molar). "Arbitary" contact time 0.5 sec. Amount of dimethyldioxane passed through 135.8 g (1.170 moles)

Reaction products	Amount obtained (in g)	Yield based on dimethyldioxane (in mole %)	
		passed through	decomposed
Isoprene	62	78.2	83.2
Isobutylene	4.2	6.4	6.9
Unsaturated alcohol (IV)	1.8	1.8	—
Recovered dimethyldioxane (I).	6.4	4.7	—
Isovaleraldehyde (VI)	0.3	0.3	0.3
4-Methyl-2,3-dihydro- α-pyran (VII)	1.2	1.0	1.1
"Carbon" on catalyst (calculated as C).	2.4	2.8	3.2
High boiling unsaturated hydrocarbons and losses.	2.2	4.8	5.3

TABLE 3

Contact Conversion of Diol (II) and Cyclic Alcohol (III) on KSD Catalyst

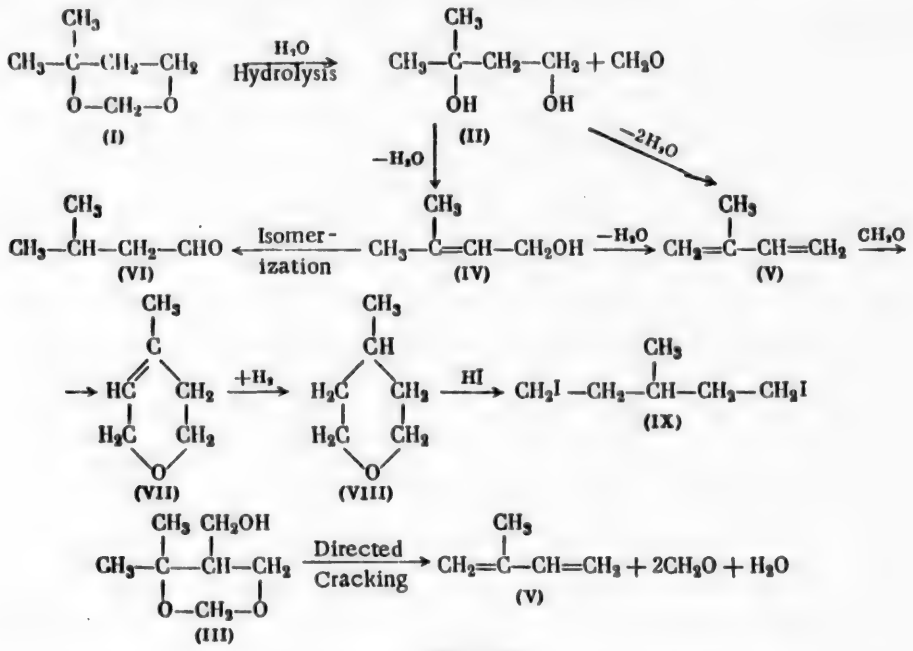
Temperature	Space velocity (ml/ ml catalyst per hour)		Arbitrary contact time (sec)	Dilution of contacted product with steam (in moles)	Conversion of contacted product to unsaturated hydrocarbon (isoprene + isobutylene) (mole %)	Amt. of isoprene in unsaturated portion of contact gas (volume %)	Yield of isoprene based on product passed through (mole %)
	contacted product	water					
			A. Conversion of Diol (II)				
350°	0.16	0.32	2.3	1 : 11	83.7	94.2	78.9
350	0.08	0.16	4.4	1 : 12	78.0	90.3	70.7
350	0.05	0.10	7.2	1 : 12	61.9	86.8	53.7
400	0.32	0.65	1.0	1 : 12	82.7	90.5	74.8
400	0.16	0.32	2.1	1 : 12	77.8	90.3	70.3
400	0.076	0.15	4.4	1 : 11	70.4	87.4	61.3
			B. Conversion of Cyclic Alcohol (III)				
350	0.17	0,32	2.3	1 : 16	42.4	94.3	39.9
350	0.08	0.15	5.0	1 : 15	44.3	83.6	37.1
350	0.04	0.07	11.1	1 : 15	39.8	68.3	27.2
400	0.36	0.67	1.1	1 : 15	42.1	93.8	39.4
400	0.17	0.32	2.2	1 : 15	49.2	90.3	44.4
400	0.08	0.15	4.7	1 : 15	49.8	78.4	39.0

In the material balance experiments the yields of formaldehyde formed as the result of reaction (1 mole of formaldehyde per mole of isoprene and 2 moles per mole of isobutylene) ranged from 90 to 93%.

Utilization of the higher boiling products from the reaction of isobutylene with formaldehyde to obtain isoprene. The products from the reaction of isobutylene with formaldehyde include, besides the main product—dimethyldioxane (I)—also the higher boiling products: diol (II) (7-10%, based on reacted formaldehyde) and the cyclic alcohol (III) (7-8%). The contact conversion of these products on the KSD catalyst, using conditions close to the conditions of cleaving the dimethyldioxane, also leads to the formation of isoprene (Scheme 2).

In Table 3 we give some data on the contact conversion of the higher boiling products under conditions close to the optimum. From these data it can be seen that diol (II) (as might be expected) is smoothly dehydrated to isoprene in a yield [75-78%, based on passed (II)] that is close to the yield of isoprene from the dimethyldioxane. The conversion of the cyclic alcohol (III) goes less smoothly; in this case the yield based on (III) passed through is reduced in half (39-44%). Because of the close boiling points of (II) and (III) it is recommended that the isolation and catalytic contacting of these products be done without separation. By processing the higher boiling products it becomes possible to increase the isoprene yield by 16-20% on the process as a whole.

Mechanism of the reaction (Scheme 2). Above we had shown (Table 1) that increasing the steam concentration in the reaction mixture leads to a substantial acceleration of the catalytic cleavage of dimethyldioxane (I). This gives us reason to believe that water takes a direct part in the reaction. In our opinion, this participation consists of water reacting with (I) on the catalyst surface, as a result of which (I) is hydrolyzed to diol (II), and then (II) dehydrates either to isoprene (V) or to unsaturated alcohol (VI).



Scheme II

The fact that the diol is absent in the reaction products does not contradict such a concept. We believe that the diol, formed as a result of the hydrolysis of (I) on the catalyst, is adsorbed on the surface; here its dehydration takes place sooner than does its desorption and escape in the gas phase. The characteristics of the KSD catalyst, which possesses simultaneous hydrolyzing and dehydrating properties, favor the reaction going in this manner. Thus, using the same catalyst and conditions close to those described above, we were able to effect the smooth hydrolysis of methylal to methanol and formaldehyde in yields exceeding 80% [6]. Using the same catalyst and the same conditions we were able to dehydrate tert-butyl alcohol quantitatively to isobutylene. In addition to the main reaction, there is also a parallel secondary reaction of the cracking of (I) to isobutylene and formaldehyde, proceeding at a slow rate at the temperatures chosen. The formation of isovaleraldehyde (VI) can be explained by the isomerization of the β-unsaturated alcohol (IV). That it is possible to isomerize such

alcohols to aldehydes in the presence of acid-type catalysts is known from the literature [7]. 4-Methyl-2,3-dihydro-α-pyran (VII) is apparently formed as the result of isoprene reacting with formaldehyde (Scheme 2) under the reaction conditions. Here we have a rarely observed case of diene synthesis with the aldehyde functioning as a dienophile component. It is indicated in the literature that the reaction of 2-methyl-1,3-pentadiene with acetaldehyde results in the formation of a dihydro-α-pyran derivative [8].

EXPERIMENTAL

A schematic diagram of the laboratory apparatus used in our work is shown in Fig. 4. Quartz tube 1 with an internal diameter of 22-25 mm served as the reactor, and was inserted in a block electric furnace 2. The catalyst (as small cylindrical pellets 2.5-5 mm in length) was placed in the middle section of the reactor to the extent of 20-40 mm. The upper part of the reactor 3 (with separate additional heat) served as a preheater to

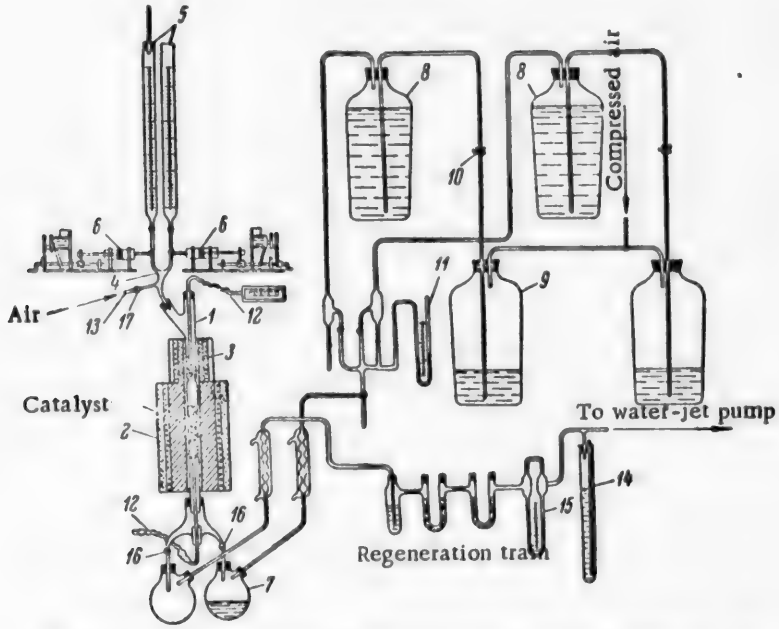


Fig. 4. Schematic diagram of the laboratory contact apparatus. Explanation in text.

vaporize the alkyldioxane and water and was filled with quartz lumps. The temperatures in the catalyst layer and at the exit of the vapors from the preheater were measured with thermocouples 12, and the temperature during the contact catalysis was kept constant within ± 2°. The reactor was connected through a T-shaped mixer 4 with two burettes 5 and two microdosers 6, serving to feed the reactants automatically. The liquid reaction products were collected in flask 7, and the gaseous products were collected in gas meters 8. The contacting was done under a slight vacuum of 15-20 mm, which was created by the overflow of brine from gas meters 8 into bottle 9, and was regulated by clamps 10 using manometer 11. At the end of the experiment the isoprene was removed from the catalyst by blowing, and was collected in receiver 7; here the receiver was placed in a water bath at 60°.

The KSD catalyst was used in the principal experiments of the present investigation. The freshly charged KSD sample was activated by treatment with a steam-air mixture (750 ml of air and 0.75 ml of water per ml of catalyst per hr) at 375° for 2 hr. A constant air feed rate was achieved by means of manostat 14 and was regulated with rheometer 15. The catalyst was regenerated periodically, every 2-4 hr during operation, by treatment with steam-air mixture at 375-400° until CO_2 was absent in the regeneration bases.

4,4-Dimethyldioxane. The technical product was redistilled through a laboratory column with an efficiency of 17 theoretical plates and had the following constants [4]: b.p. 131-133°, $n^{20}D$ 1.4239, d^{20}_4 0.9624.

The space velocity of both the dimethyldioxane and the water was expressed in milliliters of liquid passed through per ml of catalyst per hour.

The "arbitrary" contact time was calculated using the equation $\tau = \frac{V_c 273 \cdot P}{V_g T \cdot 769}$, where τ is the contact time; V_c is the catalyst volume (in ml) (here the free volume of the contact layer was taken equal to 65% of the bulk volume of the catalyst); V_g is the volume of the gases (in ml/sec) (including the dioxane and water vapors); P is the pressure (in mm of Hg); and T is the absolute reaction temperature.

Analysis procedure. The total amount of unsaturated hydrocarbons in the gas obtained after blowing out the catalyzate was determined by absorption in 84% sulfuric acid using an Orsat apparatus. The amount of isoprene in this gas was determined by absorption with maleic anhydride using a Bushmarin apparatus [9]. For a more complete characterization of the reaction products under conditions assuring better yields we ran a series of material balance experiments (see below).

Evaluation of experimental results. This was done employing the following three main criteria.

a) The extent of dimethyldioxane conversion to unsaturated hydrocarbons (isoprene and isobutylene) using the formula: $N = \frac{V \cdot a \cdot 100}{Q \cdot 22.4}$, where V is the volume of gas (in liters) (converted to standard conditions); a is the amount of unsaturated hydrocarbons in this gas; and Q is the amount of alkyldioxane passed through (in moles). This criterion characterizes the extent of conversion.

b) The yield of isoprene based on passed dimethyldioxane (in mole %) using the equation $B = \frac{V \cdot b \cdot 100}{Q \cdot 22.4}$, where b is the amount of isoprene in the gas.

c) The amount of isoprene in the unsaturated portion of the gas (in %): $C = \frac{b \cdot 100}{a}$, which characterizes the selectivity of the process.

The experiments on the contact conversion of the higher boiling reaction products and an evaluation of the experimental results were conducted in the same manner as described above.

3-Methylbutanediol (II). For the experiments we used the fraction with b.p. 107-109° (15 mm), $n^{20}D$ 1.4447, d^{20}_4 0.9872, which was isolated from the reaction products. This fraction analyzed (hydrolysis with hydroxylamine [6]) about 6% of cyclic alcohol (III). In calculating the yields this fraction was taken as being 100% diol (II). Literature data [4]: b.p. 107-109° (15 mm), $n^{20}D$ 1.4440, d^{20}_4 0.9867.

4,4-Dimethyl-5-hydroxymethyl-1,3-dioxane (III). We used the fraction with b.p. 115-120° (11 mm), $n^{20}D$ 1.4600, d^{20}_4 1.0887. According to the analysis this fraction contained 10% of the diol. Literature data [4]: b.p. 115-116° (11 mm), $n^{20}D$ 1.4644, d^{20}_4 1.0905.

Material balance experiments. In running the material balance experiments we combined the reaction products obtained from a number of experiments run under constant conditions. Here the receiver for the liquid products (7, Fig. 4) was cooled strongly (mixture of ice and salt) in order to condense the greater portion of the reaction products. The gas was analyzed in the same manner as described above. The liquid condensate was fractionated through a laboratory column with an efficiency of 70 theoretical plates. The first fraction distilled up to 35°, and consisted of isoprene with some isobutylene. The residue, composed of two layers, was separated. Dimethyldioxane (I) and unsaturated alcohol (IV) were distilled from the bottom aqueous layer as an azeotropic mixture with b.p. 92-95°. The amount of (IV) in the azeotrope was determined by bromate-bromide titration [9], while the amount of (I) was verified by hydrolysis in the presence of hydroxylamine salt [6]. The upper condensate layer from a large number of experiments was dried and then it was also fractionated; here the following fractions were collected: isoprene (b.p. 34°); fraction with b.p. 90-94°, containing 80% isovaleraldehyde (VI); fraction with b.p. 117-119°, being 4-methyl-2,3-dihydro-α-pyran (VII); and fraction with b.p. 132-135°, being dimethyldioxane (I) and unsaturated alcohol (IV). The residue with boiling point above 135° was a complex mixture of unsaturated hydrocarbons; this was combined with the other residues. The amount of formaldehyde in each of the catalyzate layers was determined separately. The amount of "carbon" on the catalyst was determined from the amount of carbon dioxide in the contact gas and in the regeneration gases [the CO_2 in the latter was determined from the increase in the weight of U-shaped tubes filled with ascarite (Fig. 1)].

Identification of reaction products. • The isoprene (V) obtained in the present process was easily isolated as a very pure product, boiling within 0.1°, and having the constants: b.p. 34°, $n^{20}D$ 1.4219, and d^{20}_4 0.6805. The adduct with maleic anhydride had m.p. 63-63.5°(from benzine).

2-Methyl-2-buten-4-ol (IV) was isolated from the fraction with b.p. 139-140° as the phenylurethan with m.p. 63-63.5° (from alcohol).

Literature data [10]: b.p. 140°; phenylurethan m.p. 63-64°.

Isovaleraldehyde (VI) was isolated from the 90-94° fraction (oil layer) as the 2,4-dinitrophenylhydrazone with m.p. 117.5-118° (from alcohol). The mixed melting point with the dinitrophenylhydrazone of authentic isovaleraldehyde was not depressed.

4-Methyl-2,3-dihydro-α-pyran (VII). Its constants were as follows.

B.p. 118.5-119°, $n^{20}D$ 1.4490, d^{20}_4 0.9116, MR_D 28.82; calc. 28.84.

Found %: C 73.20, 73.64; H 10.42, 10.32. M 98.77; hydrogen number 242; bromine number 160. $C_6H_{10}O$. Calculated %: C 73.5; H 10.30. M 98.0; hydrogen number 228.5; bromine number 163.0.

The structure of (VII) was proved by its hydrogenation to 4-methyltetrahydropyran (VIII) and subsequent ring cleavage of the latter (Scheme 2).

a) Hydrogenation of (VII). A charge of 2 g of catalyst (5% Pd on active carbon) and 17 g of (VII) was placed in the hydrogenation apparatus. The amount of hydrogen consumed was 4100 ml (0°, 760 mm). We obtained 14.9 g of 4-methyltetrahydropyran (VIII), b.p. 105-107°, $n^{20}D$ 1.4190, d^{20}_4 0.8569.

Literature data [10]: b.p. 104.5-106° (at 749 mm), $n^{20}D$ 1.4189, $d^{21.1}_4$ 0.8537.

b) Cleavage of the ring in (VIII). Twenty-five grams of P_2O_5 was charged into a round-bottomed flask fitted with a stirrer; then 70 g of 89% H_3PO_4 was added with stirring. This was followed by the addition of 106 g of KI and 11.5 g of (VIII). The mixture was heated under reflux (180°) for 3 hr. The reaction mixture was then cooled and 50 ml of water was added. The ether extract was washed with $Na_2S_2O_3$ solution and then with saturated NaCl solution. After drying, the solution was fractionally distilled to yield 3-methyl-1,5-diiodopentane (IX).

B.p. (at 4 mm) 120-121°, $n^{20}D$ 1.5870, d^{20}_4 2.039, MR_D 55.70; calc. 55.51.

Found %: C 21.39; H 3.51; I 75.6. $C_6H_{12}I_2$. Calculated %: C 21.30; H 3.58; I 75.15.

SUMMARY

1. The process for the synthesis of isoprene from the reaction products of isobutylene with formaldehyde was studied and a suitable catalyst was selected.

2. As the result of a detailed study of the reaction conditions for the contact cleavage of dimethyldioxane (the main product from the reaction of isobutylene with formaldehyde) we were able to obtain isoprene in yields as high as 75-78% based on dimethyldioxane passed through, and up to 80-85% based on decomposed dimethyldioxane.

3. The higher boiling products from the reaction of isobutylene with formaldehyde can also be subjected to contact decomposition with the formation of isoprene.

4. Both the principal and secondary reaction products obtained in the formation of isoprene were examined and identified, and a mechanism was proposed for the process that was in good agreement with the facts.

5. The high yields obtained in the process as a whole place the proposed method of synthesizing isoprene in the class of efficient processes of contemporary organic synthesis.

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N-SUBSTITUTED AMIDES OF SALICYLIC ACID AND ITS DERIVATIVES

II. MESO-ACRIDINYLAMIDE OF SALICYLIC ACID

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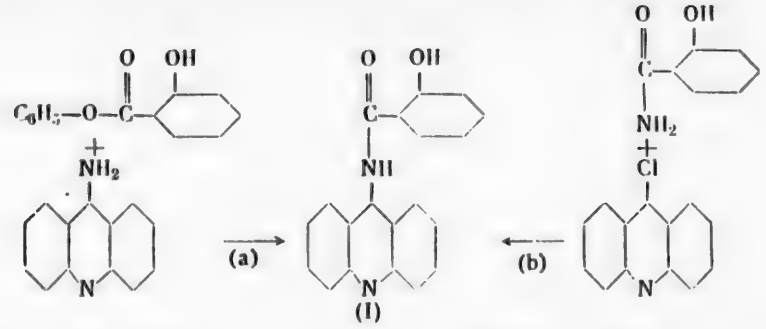
The fusion of salol or its derivatives with aromatic amines is a very convenient way [1] of obtaining various arylamides of salicylic acid. This method is also suitable for the synthesis of N-substituted amides of this acid, where heterocyclic radicals are substituted on the amino nitrogen: For example, the α-pyridylamide of salicylic acid was obtained very smoothly and in high yield from α-aminopyridine [1, 2]. We postulated that the meso-acridinylamide of salicylic acid is obtained in a similar manner from meso-aminoacridine; however, it proved that the reaction of salol with meso-aminoacridine is somewhat more complex and leads to the formation of a mixture of compounds, which differ in both chemical structure and properties and can be separated from each other by their different solubility in hot water and in aqueous alkalies.

The first indication that salol reacts with meso-aminoacridine in an unusual manner is a gradual reddening of the melt. Treatment of the melt with hot water results in the extraction of one of the reaction products which is soluble in hot water; it separates as lemon-yellow crystals when the solution is cooled. These crystals after purification melt at 279-280°. The water-insoluble residue is partially soluble in dilute aqueous alkali; acidification of the obtained solution in the cold yields a stable yellow gel; acidification in the hot yields a bright yellow precipitate, which after several recrystallizations from a mixture of benzene and pyridine melts at 267-268°. The product that fails to dissolve in the caustic is obtained as an orange powder, which can be purified only with difficulty; when this powder is dissolved in hot alcohol containing hydrochloric acid, followed by cooling of the filtered solution, it separates as handsome red needle crystals, melting above 360°.

The substance soluble in hot water and crystallizing as lemon-yellow crystals with m.p. 279-280° proved to be the salicylic acid salt of meso-aminoacridine. A precipitate of the free base separates immediately when a solution of this substance is treated with dilute alkali; salicylic acid was obtained when the filtrate from this product was evaporated and acidified. The mixed melting point of this substance with the authentic salt, obtained by mixing solutions of meso-aminoacridine and salicylic acid, was not depressed.

The second substance, which is soluble in alkali and on acidification of the warm alkaline solution separates as a yellow precipitate (after purification melting at 267-268°), proved to be the sought meso-acridinylamide of salicylic acid (I). It is possible to regard it as the primary product of the direct reaction of salol with meso-aminoacridine according to Scheme (a). The structure of this substance was confirmed by its synthesis from meso-chloroacridine and the amide of salicylic acid according to Scheme (b).

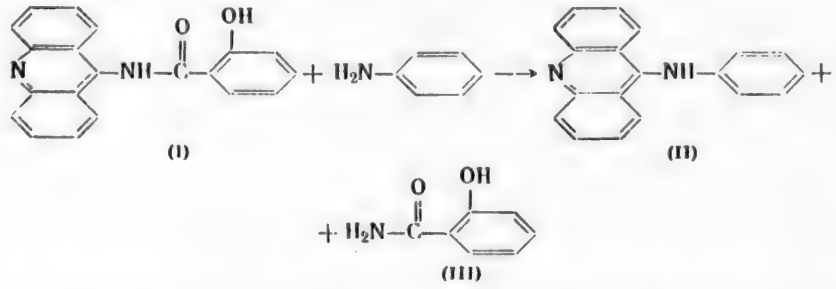
The greatest difficulties were encountered in trying to establish the structure of the third substance, remaining after treatment of the melt with hot water and aqueous alkali solution as an orange powder, which when recrystallized from alcohol acidified with hydrochloric acid is converted to red needle crystals. Treatment of the latter with alkali again yields an orange substance, which forms red-colored salts not only with hydrochloric, but



but also with other mineral acids. This substance dissolves in concentrated acids, giving a yellow color. Dilution of such a solution with water yields a red precipitate.

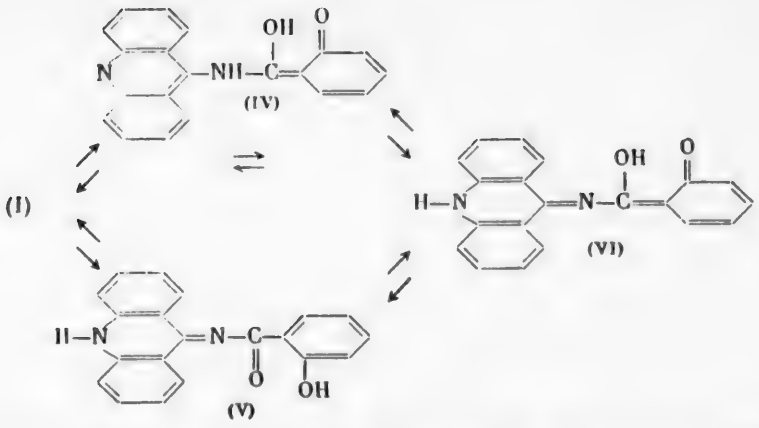
On the assumption that the orange substance is a secondary product obtained by the reaction of the first formed meso-acridinylamide of salicylic acid with the meso-aminoacridine present in the reaction mixture, we ran some special experiments in which a mixture of equimolar amounts of these authentic compounds was fused. Here we obtained an orange substance, which proved to be identical with the product isolated from the melt of salol with meso-aminoacridine. We were able to establish the structure of this substance only after we had made a detailed study of the properties of the meso-acridinylamide of salicylic acid (I). It proved that in the latter the bond between the nitrogen atom and the meso-carbon of the acridine ring is less stable than in other acylated meso-aminoacridines or in the unsubstituted amine. Thus, for example, the meso-acridinylamide of salicylic acid on long heating with 1% NaOH solution is converted to acridone. Under similar conditions meso-acetamidoacridine is hydrolyzed to yield the unsubstituted amine. The latter in turn is also stable; it is cleaved only to a slight degree with the liberation of ammonia and the formation of acridone when heated with 5N KOH solution [3].

The bond between the nitrogen atom and the meso-carbon of the acridine ring is also cleaved with comparative ease when (I) is heated with amines. In particular, when the meso-acridinylamide of salicylic acid was heated with aniline, we obtained meso-anilinoacridine (II) in high yield, which was shown to be identical with the authentic product obtained by the reaction of aniline with meso-chloroacridine (IV)[4]. This indicates that when the meso-acridinylamide of salicylic acid (I) is heated with aniline there occurs a cleavage of the bond between the nitrogen and the meso-carbon of the ring and the aniline displaces salicylamide (III) from (I).



Actually, we were able to detect the unsubstituted salicylamide (III) in the solution obtained from the heating of the melt with water. Other amides of salicylic acid, for example, the phenylamide (salicylanilide), do not react in this manner and remain unchanged when heated with aniline.

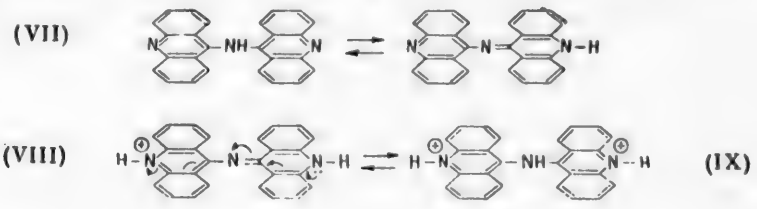
We explain the relative instability of the bond between the nitrogen atom and the meso-carbon of the acridine ring of the acridinylamide of salicylic acid as due to a reciprocal influence of the two groupings in the given compound (I). Since in this compound it is possible for tautomerism to exist both in the salicyloyl portion of the molecule, with the formation of the ortho-quinoid tautomeric form (IV), and in the acridine portion, with the formation of the acridone-imino tautomeric form (V), then a simultaneous reciprocally induced tautomerism with the appearance of form (VI), in which a system of conjugated bonds exists, is the most probable. The bright yellow color of the given acyl derivative can also be explained in this manner.



From what has been said above it follows that union between the nitrogen atom and the meso-carbon is accomplished chiefly through the double bond, where the compound, similar to amino compounds of analogous structure, is capable of being cleaved with comparative ease. Along with this we postulated that the orange product (both that isolated by us from the products of the reaction of salol with meso-aminoacridine and that obtained by the reaction of the meso-acridinylamide of salicylic acid with meso-aminoacridine) was formed as the result of the latter displacing the salicylamido grouping from the acridinylamide of salicylic acid and is di(meso-acridinyl)amine (VII). Actually, we were able to find a substantial amount of the amide of salicylic acid in the aqueous filtrates obtained from washing the reaction mixture with hot water.

To prove conclusively the above made postulation, we condensed meso-aminoacridine with meso-chloroacridine and again obtained an orange substance, which proved to be identical with the compound described above and formed bright red salts with mineral acids.

The color of the given amine and especially of its salts deserves consideration. The color of the amine can be explained by the fact that in di(meso-acridinyl)amine (VII) it is possible to have tautomerism in each of the acridine rings with the formation of forms having an acridone-imino structure.



In salt formation, the same as in the aminotriphenylmethane dye series, di(meso-acridinyl)amine (VII) forms with 1 equivalent of acid salts that are stable to hydrolysis. Here complex cation (VIII) is formed, in which the positive charge is distributed along the conjugated system between the terminal nitrogens, and this serves to explain the deep color of the salts. When treated with an excess of concd. acid the substance (VII), as the result of forming the diacid salt (IX), goes into solution, which has a yellow color. Dilution of such a solution with water again gives the red monoacid salt as a precipitate.

In its structure, di(meso-acridinyl)amine can be compared not only with the aminotriphenylmethane dyes, but also with the indamines. For a secondary amine containing heterocyclic rings to have such a color deserves consideration and further study.

EXPERIMENTAL•

A mixture of 9.8 g (0.046 mole) of salol and 5.8 g (0.03 mole) of meso-aminoacridine was heated for 3 hr at 150-160°. The original orange melt gradually changed to a dark red glassy mass, which with further heating decomposed into individual lumps.

•With the assistance of M. M. Rybakova and L. N. Fedorova.

1. Salicylic acid salt of aminoacridine. a) Isolation from the melt. The salt of salicylic acid with meso-aminoacridine was extracted completely by boiling the melt 4 times with 50-ml portions of water. The aqueous filtrate on cooling deposited 1.1 g of a lemon-yellow crystalline precipitate with m.p. 250-255°. Two recrystallizations from hot water raised the melting point of the compound to 279-280°.

b) Preparation from the components. The salicylic acid salt of meso-aminoacridine was obtained by mixing solutions of equimolar amounts of meso-aminoacridine and salicylic acid. The salt, isolated as lemon-yellow crystals, had m.p. 280°. The mixed melting point with the salt isolated from the melt was not depressed.

2. Acridinylamide of salicylic acid. a) Isolation from the melt. The reddish brown residue, insoluble in hot water, was triturated in a mortar with 50 ml of a 1% NaOH solution; the obtained mixture was brought to the boil and kept at 100° for 1 hr, after which it was filtered and the precipitate treated twice more in a similar manner. Acidification of the cold alkaline solution with either hydrochloric or acetic acid gave a stable yellow gel. To obtain a solid product the acidification with hydrochloric acid was done at 70-75°. Here 3.2 g of an intensely yellow amorphous precipitate with m.p. 254° was obtained. After precipitation with acetic acid from alcoholic alkaline solution the compound had m.p. 265°. Two recrystallizations from a mixture of pyridine and benzene raised the melting point to 267-268°.

b) Preparation from meso-chloroacridine and salicylamide. A solution containing 10.65 g (0.05 mole) of meso-chloroacridine in 500 ml of benzene heated to the boil was mixed with a solution of 8.00 g (0.06 mole) of salicylamide in 300 ml of benzene, also heated to the boil. The reaction mixture was left on a boiling water bath until the formation of a precipitate ceased (3-6 hr). The precipitate was filtered and washed on the filter with benzene until the wash liquor was colorless. Yield 5.6 g. The product was suspended in alcohol and the mixture was heated to the boil, after which caustic solution was added in drops. The free base was isolated from the alcoholic alkaline solution by the addition of acetic acid. From 5.6 g of hydrochloride we obtained 4.65 g of the free base with m.p. 246°. After a second reprecipitation from alcoholic alkaline solution with acetic acid the melting point was raised to 265°. The mixed melting point with the acridinylamide of salicylic acid obtained from the melt was not depressed.

Found % N 8.83, 9.05. $C_{20}H_{14}O_2N_2$. Calculated % N 8.92.

c) Conversion of meso-acridinylamide of salicylic acid to acridone. After refluxing 1 g of the acridinylamide of salicylic acid with 50 ml of a 1% alcohol solution of sodium hydroxide for 3 hr we obtained 0.57 g of a bright yellow flocculent precipitate, insoluble in both benzene and acetone. The obtained substance sublimed when heated to 250°. In a sealed capillary it melted above 300°. The mixed melting point with authentic acridone was not depressed.

d) Conversion of meso-acridinylamide of salicylic acid to meso-anilinoacridine. A mixture of 3 g (about 0.01 mole) of the meso-acridinylamide of salicylic acid and 6 ml of aniline, taken in excess, was heated under reflux in a sand bath for 3 hr at 180-190° and for 1 hr at 200-210°. After removal of the excess aniline by steam distillation, the aqueous filtrate deposited 2 g of a yellowish precipitate with m.p. 143°. Recrystallization from water gave colorless needles with m.p. 145°. The mixed melting point with authentic salicylamide, melting at 145°, was not depressed. The water-insoluble dark brown residue, weighing 4.9 g, was recrystallized from alcohol to give a compound with m.p. 230.5°. The product separates as yellow needles with m.p. 298° if recrystallized from hot alcohol containing hydrochloric acid. The product obtained from meso-chloroacridine and aniline [4], has the same properties. The mixed melting point of these two compounds was not depressed.

Di(mesoacridinyl)amine. a) Isolation from the melt. The residue remaining after treatment of the melt with hot water and alkali solution was added to 100 ml of boiling alcohol and then acidified with hydrochloric acid to Congo red. The precipitate dissolved completely, and the solution on cooling deposited 5.1 g of a bright red crystalline precipitate. The substance melts above 350-360°.

b) Preparation from the acridinylamide of salicylic acid. One gram of the acridinylamide of salicylic acid (0.003 mole) was fused for 3 hr at 150-160° with 1.2 g (0.006 mole) of meso-aminoacridine. The obtained dark red melt was treated with hot water and with caustic solution. The dark orange precipitate (2.3 g) was dissolved in 50 ml of boiling alcohol containing hydrochloric acid. The solution on cooling deposited a bright red crystalline precipitate, which did not melt at 350°.

c) Preparation from meso-chloroacridine and meso-aminoacridine. A mixture of 2.13 g (0.01 mole) of meso-chloroacridine and 1.94 g (0.01 mole) of meso-aminoacridine was heated at 150-160° for 3 hr. The obtained dark red melt was treated with hot water and then with caustic solution. The dark orange residue (3.6 g) was dissolved in 75 ml of boiling alcohol containing hydrochloric acid. The solution on cooling deposited a bright red crystalline precipitate that failed to melt at 350°.

Found %: N 10.33, 10.28; Cl 8.50, 8.47. $C_{26}H_{17}N_3 \cdot HCl$. Calculated %: N 10.30. Cl 8.95.

d) Conversion of the salt to the free base. A boiling solution containing 1 g of the salt in 200 ml of alcohol was treated with 1% NaOH solution until all of the salt had converted to the alcohol-insoluble free base. After refluxing for 1 hr, the precipitate was filtered and washed on the filter with water. Yield 0.9 g.

Found %: N 10.80, 10.78. $C_{26}H_{17}N_3$. Calculated %: N 11.32.

SUMMARY

1. The fusion of salol with meso-aminoacridine gave the meso-acridinylamide of salicylic acid, the structure of which was proved by its synthesis from meso-chloroacridine and salicylamide.

2. Together with the meso-acridinylamide of salicylic acid we also obtained di(meso-acridinyl)amine, which forms bright red onium salts with acids. This amine is formed as a result of secondary reaction between the initially formed amide and meso-aminoacridine. The structure of this amine was confirmed by its synthesis from meso-chloroacridine and meso-aminoacridine.

3. The meso-acridinylamide of salicylic acid reacts with other amines with the cleavage of salicylamide and the formation of the corresponding substituted meso-aminoacridine.

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REACTION OF AMINES OF ANTHRAQUINONE SERIES WITH DIKETENE

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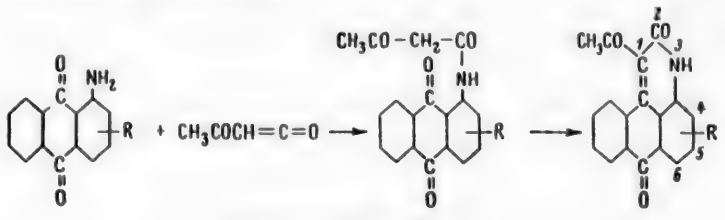
Aromatic amines react easily with diketene, forming arylides of acetoacetic acid [1]. The dependence of this reaction on the basicity of the amine was demonstrated by Lyashenko and Sokolova [2] on eight examples, and enabled one of us to extent to ketene the concepts developed to explain the acylation reaction in general. According to the developed mechanism, the success of the reaction is determined by the insertion of an unpaired pair of electrons from the nitrogen atom of the amine into the electron void of the carbon atom, formed as the result of polarization of the C = O double bond [3, 5].

Aromatic amines with a comparatively large basicity constant (anisidines, toluidines, aniline) react with diketene in the presence of solvents [4] and even in water [5], whereas less basic amines (o-nitroaniline, carbazole, diphenylamine) require the use of catalysts [6] for successful reaction.

As was shown in the present investigation, amines of the anthraquinone series also react with diketene, but here the conditions needed to obtain reaction are quite drastic. A relatively higher reactivity of the more basic amines was also observed in the anthraquinone series. Thus, secondary aliphatic-aromatic amines react with diketene under milder conditions and the reaction, as will be shown below, goes further than in the case of the primary amines.

In investigating the properties of 1-acetoacetylaminoanthraquinone it was revealed that the product under the influence of dilute alkalies or of heat loses a molecule of water and is converted to the anthrapyridone derivative.• Naturally this aroused a heightened interest and caused attention to be concentrated on the α-derivatives of the aminoanthraquinone. It was soon found that the reaction of 1-aminoanthraquinone derivatives with diketene is a general one, the same as the reaction for the closure of the pyridone ring in the obtained acetoacetyl derivatives. We were able to synthesize a number of acetoacetyl and anthrapyridone derivatives from 1-aminoanthraquinone, 2-chloro-1-aminoanthraquinone, 2-methyl-1-aminoanthraquinone, 1-amino-2-anthraquinonesulfonic acid, 1-amino-4-chloroanthraquinone, and the 1,4- and 1,5-diaminoanthraquinones. The dianthrapyridone derivatives were obtained in the last two cases. The acetoacetyl derivatives were obtained either by heating the amine in excess diketene at at 110-130°, or in pyridine solution, in some cases in the cold. Closure of the pyridone ring was effected as mentioned above, by treatment with aqueous NaOH solution with heating or even in the cold. The reaction went in accordance with the scheme:

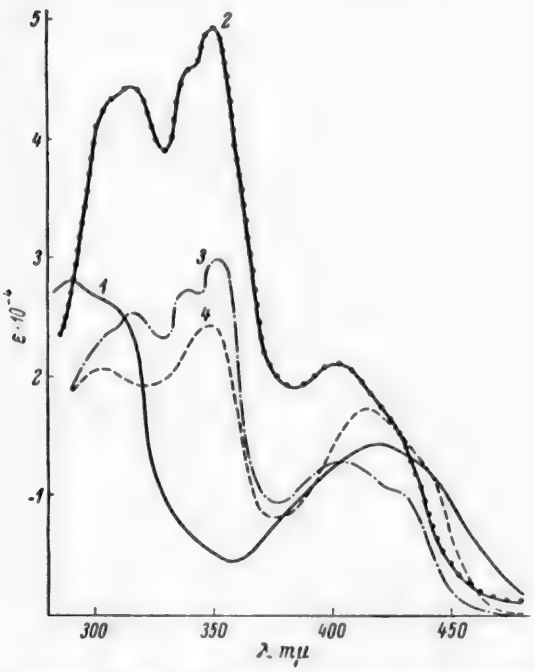


•This observation was made by N. A. Kirzner in 1948.

The greatest reactivity was shown by 2-methyl-1-aminoanthraquinone and the diaminoanthraquinones, which apparently coincides with the relatively greater basicity of these amines. Since extremely fast dyes [7] are encountered among the pyridone derivatives of anthraquinone, and having in mind the possibility of obtaining more highly colored compounds, we took as the starting materials the secondary aliphatic-aromatic and aromatic amines 1-methylaminoanthraquinone, 4-bromo-1-methylaminoanthraquinone, 1-phenylamino anthraquinone, and 4-phenylamino-1-methylaminoanthraquinone.

All of the enumerated amines react with diketene under comparatively mild conditions, with the exception of 1-phenylaminoanthraquinone, which because of its lower basicity required the use of more drastic conditions.

However, in contrast to the derivatives of 1-aminoanthraquinone, the reaction result is not the formation of the acetoacetyl, but instead is the immediate formation of the anthrapyridone derivatives. The use of milder conditions failed to change the results: The reaction either did not go at all, or it went all the way to the anthrapyridone derivatives. We were able to establish the structure of the end reaction products by comparing the absorption spectra of the synthesized compounds with the absorption spectra of 1-acetoacetylaminoanthraquinone and 1-acetylanthrapyridone. The absorption curves of all of the anthrapyridone derivatives (see figure) show a characteristic absorption maximum at a wavelength of about 350 mμ, whereas the acetoacetylaminoanthraquinone shows minimum absorption in the same region.



Absorption curves of acetoacetylaminoanthraquinone and some acetylanthrapyridone derivatives. 1) Acetoacetylaminoanthraquinone (in chlorobenzene; c 1.63 × 10^{-4} M); 2) 1-acetylanthrapyridone (in alcohol, in the presence of caustic; c 5.76 × 10^{-5} M); 3) 1-acetyl-N-methylanthrapyridone (in chlorobenzene; c 1.65 × 10^{-4} M); 4) 6-bromo-1-acetyl-N-methylanthrapyridone (in chlorobenzene; c 1.64 × × 10^{-4} M).

In addition, by reacting acetoacetic ester with the starting amines under the conditions described in the literature [8] we were able to obtain the authentic anthrapyridone derivatives, which proved to be identical with those obtained by us. Finally, the obtained anthrapyridone derivatives are not hydrolyzed by sulfuric acid and do enter into the azo-coupling reaction in pyridine solution. These reactions, as is known, are characteristic for acetoacetyl derivatives of aminoanthraquinone.

The results of reacting diketene with 1-methylamino-4-phenylaminoanthraquinone seem interesting to us. As was to be expected, this compound, having two amino groups of different basicity, reacted only via the more basic methylamino group. This was shown by the counter synthesis of 6-phenylamino-1-acetyl-N-methylanthrapyridone from 6-bromo-1-acetyl-N-methylanthrapyridone and aniline, by the aramination technique [9]. The product dissolves in acetone with a bright reddish-violet color, and can be used to dye acetate rayon [10].

EXPERIMENTAL

1. 1-Acetoacetylaminoanthraquinone•. a) To 11.16 g of 1-aminoanthraquinone in 120 ml of pyridine was added at room temperature (water bath), with stirring, 5.04 g of 98.8% diketene. After 1-1.5 hr of vigorous stirring, the obtained yellow crystals were filtered and washed with hot water until the odor of pyridine had disappeared. The yield of dry product was 12.9 g (84%); m.p. 169-170°. Dilution of the filtrate with water gave an additional 0.5-0.6 g of substance with m.p. 165° (the compound was recrystallized from acetone).

•The work with the primary aminoanthraquinone derivatives was done by N. A. Kirzner.

b) A mixture of 2.23 g of 1-aminoanthraquinone and 1.02 g of diketene was heated under reflux in a glycerin bath to 135° and kept at this temperature for 30 min. Then the mixture was cooled to 50° and 5 ml of toluene was added. The obtained precipitate was filtered and washed first with toluene, and then with ether. Yield 2.99 g (97%); m.p. 170-171° (from acetone).

Found %: C 70.28, 70.41; H 4.42, 4.36; N 4.68, 4.65. $C_{18}H_{13}O_4N$. Calculated %: C 70.35; H 4.26; N 4.56.

2. 1-Acetylanthrapyridone. A solution of 1 g of 1-acetoacetylaminoanthraquinone in 100 ml of warm 2% NaOH solution was filtered, and the filtrate was treated with acetic acid until acid. The light yellow crystalline precipitate was filtered, washed with water, and dried. Yield 0.89 g (95%); m.p. 285-287°. After recrystallization from acetone, bromobenzene or glycol diacetate, m.p. 296°.

Found %: C 74.47, 74.65; H 3.82, 3.88; N 4.90, 4.97. $C_{18}H_{11}O_3N$. Calculated %: C 74.73; H 3.84; N 4.84.

The product is soluble in dilute alkalies and ammonia, and in concd. sulfuric acid. The compound separates in unchanged form when the concd. sulfuric acid solution is diluted. Oxidation of the compound with alkaline permanganate solution converts it to the carboxylic acid, which decarboxylates easily with the formation of anthrapyridone.

3. 1-Acetoacetylamino-2-methylanthraquinone was obtained from 2.37 g of 1-amino-2-methylanthraquinone and 2.55 g of 98.8% diketene by the method described in 1 b, at 130-135°, for several minutes. After cooling to 40°, the reaction mass was diluted with 5 ml of benzene and filtered. Yield 2.6 g (81%); m.p. 138° (from acetone).

Found %: C 71.17, 71.12; H 4.78, 4.80; N 4.62, 4.58. $C_{19}H_{15}O_4N$. Calculated %: C 71.02; H 4.70; N 4.36.

The product is soluble in dilute alkalies, ammonia, and concd. sulfuric acid. When heated it loses water and is converted to the anthrapyridone derivative.

4. 1-Acetyl-4-methylanthrapyridone was obtained in the same manner as 1-acetylanthrapyridone, as described in 2. We obtained 0.93 g of 1-acetyl-4-methylanthrapyridone from 1 g of 1-acetoacetylamino-2-methylanthraquinone. M.p. 315° (from glacial acetic acid or glycol diacetate).

Found %: C 75.13, 75.10; H 4.38, 4.42; N 4.74. $C_{19}H_{13}O_3N$. Calculated %: C 75.22; H 4.32; N 4.62.

5. 1-Acetoacetylamino-2-chloroanthraquinone was obtained by the method described in 1. The reaction was run with 5.15 g of 1-amino-2-chloroanthraquinone and 2.55 g of 98.8% diketene at 145-150° for 10 min. Dilution of the melt with 10 ml of acetone gave 5.1 g (74.7%) of 1-acetoacetylamino-2-chloroanthraquinone. Yellow crystalline powder with m.p. 160° (from dioxane or alcohol).

Found %: C 63.23, 63.31; H 3.62, 3.48; N 4.35, 4.40; Cl 10.30, 10.35. $C_{18}H_{12}O_4NCl$. Calculated %: C 63.26; H 3.54; N 4.10; Cl 10.37.

6. 1-Acetyl-4-chloroanthrapyridone was obtained by the method described in 2. We obtained 0.91 g (96%) of 1-acetyl-4-chloroanthrapyridone from 1 g of 1-acetoacetylamino-2-chloroanthraquinone. Brownish-yellow crystalline powder with m.p. 312° (from dilute acetic acid or glycol diacetate).

Found %: C 66.75, 66.86; H 3.27, 3.19; N 4.42, 4.56; Cl 10.89, 10.92. $C_{18}H_{10}O_3NCl$. Calculated %: C 66.78; H 3.11; N 4.32; Cl 10.95.

7. Sodium 1-acetoacetylamino-2-anthraquinonesulfonate was obtained from 6.5 g of sodium 1-amino-2-anthraquinonesulfonate and 1.86 g of 98.8% diketene in 200 ml of water in the presence of 10 ml of pyridine at room temperature for 2 hr. The diketene was added slowly. The reaction product was precipitated by the addition of an equal volume of saturated sodium chloride solution.

The red gelatinous precipitate changed (more rapidly if warmed gently) to golden leaflets. The product was filtered, washed with sodium chloride solution, then with ethanol, and finally with ether. Yield 6.64 g (81%). Recrystallization from dilute methanol gave the compound as golden-bronze leaflets (did not melt).

Found %: C 52.93, 52.86; H 3.01, 3.52; N 3.65, 3.52; S 7.75, 7.79. $C_{18}H_{12}O_7NSNa$. Calculated %: C 52.81; H 2.96; N 3.42; S 7.83.

8. Sodium 1-acetyl-4-anthrapyridonesulfonate. A solution of 1 g of sodium 1-acetoacetylamino-2-anthraquinonesulfonate in 50 ml of 2% NaOH solution was heated at 80-90° for 10-15 min. The reaction solution was cooled and the reaction product was isolated by the addition of ethanol, followed by filtration. Yield 0.7 g (73%). Recrystallization from dilute ethanol gave the compound as a golden-yellow crystalline powder.

Found %: C 55.07, 55.16; H 2.64, 2.71; N 3.85, 3.74; S 8.08, 8.13. $C_{18}H_{10}O_6NSNa$. Calculated %: C 55.24; H 2.58; N 3.58, S 8.19.

9. 1-Acetoacetylamino-4-chloroanthraquinone was obtained by the method described in 1, from 5.15 g of 1-amino-4-chloroanthraquinone and 2.55 g of 98.8% diketene, at 130°, for 15-20 min. Addition of acetone to the reaction solution to precipitate the product gave 5.7 g (83.5%) of 1-acetoacetylamino-4-chloroanthraquinone with m.p. 162° (from toluene or xylene).

Found %: C 63.10, 63.35; H 3.56, 3.50; N 4.29, 4.36; Cl 10.35, 10.32. $C_{18}H_{12}O_4NCl$. Calculated %: C 63.26; H 3.54; N 4.10; Cl 10.37.

10. 1-Acetyl-6-chloroanthrapyridone was obtained by the method described in 2. We obtained 0.92 g of 1-acetyl-6-chloroanthrapyridone from 1 g of 1-acetoacetylamino-4-chloroanthraquinone. Lustrous golden-yellow leaflets with m.p. 317° (from glycol diacetate).

Found %: C 66.71, 66.98; H 3.27, 3.32; N 4.32, 4.61; Cl 10.83, 10.90. $C_{18}H_{10}O_3NCl$. Calculated %: C 66.78; H 3.11; N 4.32; Cl 10.95.

11. 1,4-Di(acetoacetylamino)anthraquinone was obtained from 5.0 g of 1,4-diaminoanthraquinone and 5.04 g of 98.8% diketene by the method of 1 b, at 100-110°, for 10-15 min. The reaction product was precipitated at 50° by the addition of 15 ml of acetone. Yield 7.5 g (88%), m.p. 192° (from glycol diacetate).

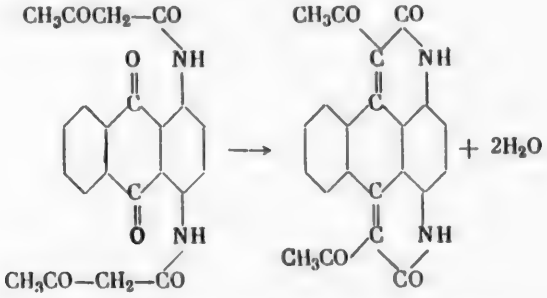
Found %: C 65.11, 65.21; H 4.56, N 7.10, 7.18. $C_{22}H_{18}O_6N_2$. Calculated %: C 65.02; H 4.45; N 6.89.

1,4-Di(acetoacetylamino)anthraquinone dissolves in concd. sulfuric acid with a green color, changing to a yellow-brown.

12. 1,8-Diacetylanthradipyridone was obtained by the method described in 2. Hydrochloric acid was used to isolate the reaction product. We obtained 0.9 g of product from 1 g of 1,4-di(acetoacetylamino)anthraquinone. Recrystallization from glacial acetic acid or mesityl oxide gave a product that does not melt when heated to 340°.

Found %: C 71.20, 71.55; H 4.03, 4.12; N 7.87, 7.73. $C_{22}H_{14}O_4N_2$. Calculated %: C 71.35; H 3.81; N 7.56.

The reaction goes according to the scheme:



13. 1,5-Di(acetoacetylamino)anthraquinone was obtained by the method of 1 b from 5.0 g of 1,5-diaminoanthraquinone and 5.04 g of 98.8% diketene, at 140-145°, for 15-20 min. Isolation of the reaction product by the addition of 10 ml of acetone gave 6.74 g (83.0%) of 1,5-di(acetoacetylamino)anthraquinone. The compound was obtained as an orange-yellow crystalline powder with m.p. 226-227° (from glycol diacetate).

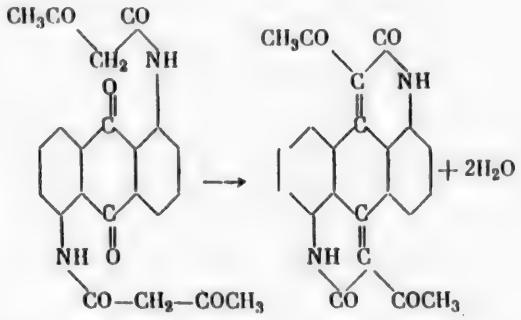
Found %: C 65.15, 65.20; H 4.52, 4.58; N 7.05, 7.21. $C_{22}H_{18}O_6N_2$. Calculated %: C 65.02; H 4.45; N 6.89.

1,5-Di(acetoacetylamino)anthraquinone is difficultly soluble in acetone, alcohol, and chloroform, more soluble in xylene, and readily soluble in glycol diacetate. It dissolves in concd. sulfuric acidgiving a wine-red color, gradually changing to a yellow

14. 1,7-Diacetylanthrapyridone was obtained by the method described in 2. Hydrochloric acid was used to isolate the reaction product from the alkaline solution. The yield of 1,7-diacetylanthrapyridone from 1 g of 1,5-di(acetoacetylamino)anthraquinone was 0.91 g. Recrystallization from acetic acid gave the compound as yellow crystals that failed to melt when heated to 330°.

Found %: C 71.32, 71.46; H 3.85; 3.96; N 7.67, 7.73. $C_{22}H_{14}O_4N_2$. Calculated %: C 71.35; H 3.81; N 7.56.

The reaction goes according to the scheme:



15. 1,8-Di(acetoacetylamino)anthraquinone was obtained by the method of 1 b from 5.0 g of 1,8-diaminoanthraquinone and 5.04 g of 98.8% diketene, at 110-120°, for 5-10 min. The addition of 10 ml of acetone to the melt, cooled to 50°, gave 5.4 g (69.4%) of yellow 1,8-di(acetoacetylamino)anthraquinone with m.p. 172°. The brownish-yellow crystalline product melted at 179-180° (from acetone).

Found %: C 65.10, 65.07; H 4.47, 4.55; N 7.02, 7.11. $C_{22}H_{18}O_6N_2$. Calculated %: C 65.02; H 4.45; N 6.89.

16. 1-Acetyl-N-methylanthrapyridone• was obtained from a mixture of 1 g of 1-methylaminoanthraquinone and 3.6 ml of 97% diketene in 35 ml of pyridine, at 50-60°, for 1 hr. The product was precipitated by the addition of 15 ml of ethanol. After 2 hr the product was filtered, washed with alcohol, and dried. Yield 2.0 g (78%); m.p. 287-288° (with decompn.) (from pyridine).

Found %: C 75.44, 75.11; H 4.38, 4.41; N 4.87, 4.79. $C_{19}H_{13}O_3N$. Calculated %: C 75.24; H 4.32; N 4.62.

17. 1-Acetyl-N-methyl-6-bromoanthrapyridone was obtained by the method described in 16 from 2 g of 1-methylamino-4-bromoanthraquinone and 3.6 ml of 97% diketene in 35 ml of pyridine. After precipitation with 20 ml of ethanol and allowing to stand for a day we obtained 1.81 g (75%) of substance. After recrystallization from a mixture of pyridine and ethanol (3 : 2), and then from chlorobenzene, the m.p. was 242°.

Found %: C 59.90, 59.55; H 3.68, 3.52; Br 21.32, 21.17. $C_{19}H_{12}O_3NBr$. Calculated %: C 59.70; H 3.17; Br 20.91.

18. 1-Acetyl-N-phenylanthrapyridone. a) To a solution of 0.8 g of 1-phenylaminoanthraquinone [11] in 10 ml of pyridine was added dropwise at 75-80°, with stirring, 3 ml of 97% diketene in 1 hr. Then the temperature of the reaction mass was raised to 85° and another 3.5 ml of diketene was added in 1.5 hr. After 15 min, 10 ml of ethanol was added. After allowing to stand, 10 ml of solvent was vacuum distilled and another 10 ml of ethanol was added. After 2 days a product separated from the solution; this was filtered, washed with alcohol, then with carbon tetrachloride, and finally with ether. Yield 0.37 g (38%). After recrystallization from a mixture of acetone and alcohol (3 : 1), and then from acetone, the m.p. was 241-242°.

• The syntheses from the secondary amines were run by Yü Fyei-pei with consultation by L. S. Efros, to whom we express out thanks.

b) A mixture of 0.8 g of 1-phenylaminoanthraquinone and 9.6 g of diketene was heated to 100-102°, and then the mixture was kept at this temperature for 2 hr. After this about 3 ml of diketene was removed by vacuum distillation, and the residual solution was diluted with 10 ml of ethanol. After standing for a day the obtained golden-orange crystals were filtered, washed with alcohol, then with carbon tetrachloride, finally with ether, and dried. We obtained 0.52 g (53%) of product; m.p. 242-243° (from a 3 : 1 mixture of acetone and alcohol).

Found %: C 78.96, 79.18; H 4.12, 4.17. $C_{24}H_{15}NO_3$. Calculated %: C 78.89; H 4.14.

19. 1-Acetyl-N-methyl-6-phenylaminoanthrapyridone. a) From 1-methylamino-4-phenylaminoanthraquinone [12]. The product was obtained by the method described in 16. A mixture of 1.2 g of 1-methylamino-4-phenylaminoanthraquinone and 1 ml of diketene in 10 ml of pyridine was heated at 50-53° for 45 min. After adding 30 ml of ethanol and 30 ml of water, the mixture was allowed to stand for 3 days, after which the violet precipitate was filtered, washed with alcohol, and then with ether. Yield 1.14 g (79%). After chromatographing on aluminum oxide, followed by recrystallization from a mixture of ethanol and benzene and then from acetone, we obtained lustrous purple needles with m.p. 213°.

Found %: C 75.91, 76.40; H 4.61, 4.70; N 7.69, 7.79. $C_{25}H_{18}O_3N_2$. Calculated %: C 76.10; H 4.60; N 7.10.

b) From 1-acetyl-N-methyl-6-bromoanthrapyridone: A mixture of 2 g of 1-acetyl-N-methyl-6-bromoanthrapyridone, 8 ml of distilled aniline, 10 ml of isobutyl alcohol, 0.06 g of anhydrous sodium acetate and 0.02 g of copper powder was heated under reflux for 7 hr. The solvents were steam-distilled, while the precipitate was refluxed with ethanol for 1 hr. Filtration, followed by washing with alcohol and then with water, and drying, gave 2 of product; m.p. 212-213° (from acetone). The mixed melting point with the product obtained by method "a" was not depressed.

SUMMARY

1. 1-Aminoanthraquinone and its derivatives react with diketene, forming acetoacetyl derivatives of the aminoanthraquinone. The more basic the amine, the easier it is for reaction to take place.

2. The obtained acetoacetyl derivatives when treated with dilute caustic alkalies are converted to the corresponding 1-acetylanthrapyridones. The same thing may be achieved by heating the acetoacetyl derivatives to a high temperature.

3. 1-Methylaminoanthraquinone and its derivatives react more easily with diketene than does 1-aminoanthraquinone: The reaction cannot be made to stop at the acetoacetylaminoanthraquinone stage; here the anthrapyridone derivatives are obtained immediately as the reaction result. The reaction goes more easily the more basic the starting amine.

4. The obtained acetoacetyl and anthrapyridone derivatives can be used as dyes for acetate rayon, or as intermediates for the synthesis of more complex dyes.

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*Chemical Abstracts.

THE STRUCTURE AND TRANSFORMATIONS

OF DIAZO COMPOUNDS

XIII. QUANTITATIVE CHARACTERIZATION OF THE ACID-BASE PROPERTIES OF p-NITRODIAZOBENZENE

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As we have already indicated [1], the calculations made earlier by a number of investigators [2-5] for the acid and base constants of various types of diazo compounds were based on erroneous premises; the present authors were faced with the problem of determining the values of these constants taking into consideration some new experimental data [1, 6].

Below we give a calculation of some of the physicochemical constants of p-nitrodiazobenzene.•

As has already been mentioned [1, 6], the value of the hydrolysis constant of the diazo cation, equal to $K = 6.3 \times 10^{-6}$, was determined by us as the ratio

$$K = \frac{[RN_2O^-][H^+]^2}{[RN_2^+]}$$

The concentrations of the p-nitrophenyldiazo cation and p-nitrophenyldiazo anion were determined by us using both gravimetric and quantitative spectral analysis [1, 6]. The values of the hydrolysis constants, calculated from the data of the gravimetric and spectral analyses, differed on the order of 0.1.

Extrapolation of the pH values at the equivalent points of the second jump in the potential on the neutralization curves of the strongly alkaline aqueous solutions of the potassium salt of p-nitrodiazobenzene, obtained in the titration of such solutions at different rates [1], to zero time gives a pH value of 3.8, coinciding with the value for an 0.01 M solution of the nitrosaminic acid, determined earlier by I. V. Grachev.

The addition of acid to the diazo anion can lead to the simultaneous formation of two substances—the amphoteric diazohydroxide and the nitrosamine.

$$RN_2O^- + H_3O^+ \rightleftharpoons \begin{cases} R{-}N{=}N{-}OH + H_2O \\ R{-}NH{-}NO + H_2O \end{cases}$$

Experimentation reveals that the rapid acidification of a cold solution of an alkali salt of p-nitrodiazobenzene results in the deposition of a precipitate of an unstable yellow crystalline substance which is incapable

• The data of the given calculation relate to a temperature of 11°.

of azo-coupling. This substance is probably the nitrosamine, since the diazohydroxide under these conditions should be capable of rapid cleavage of the hydroxyl and formation of the diazo cation, which is capable of azo-coupling. The spectral analyses also support this viewpoint.

As a result, we have reason to believe that a pH of 3.8, characterizing the state of the system in the initial moment, relates to the solution of the nitrosaminic acid. From this we obtain the acidity constant of the nitrosaminic acid.

$$K_a = \frac{[H^+]^2}{c} = \frac{10^{-3.8 \cdot 2}}{10^{-2}} = 10^{-5.6} = 2.5 \cdot 10^{-6}$$

It is easy to verify the validity of the calculation given above if we start with the experimentally found pH value of a 0.01 M solution of the potassium salt of p-nitrodiazobenzene, equal to 8.9. Since hydrolysis of the salt yields (although in very small amounts) a tautomeric mixture of the diazohydroxide and nitrosaminic acid, calculation[7]should give a constant that relates to the weaker acid. In determining which of the two acids isthe weaker, it should be kept in mind that O-acids are usually much stronger than N-acids, and consequently the nitrosaminic acid should be weaker than the diazoic acid. However, the presence of an acidifying nitroso group in the nitrosaminic acid and a tendency to cleave the hydroxyl in the diazohydroxide make it possible to assume a situation where the nitrosaminic and diazoic acids prove to be close in strength. Calculation in such case should give a constant that simultaneously characterizes both acids (with only a slight degree of error). As a result, calculation [8] in either case

$$pH = 0.5pK_W + 0.5pK_a + 0.5 \lg c$$

$$8.9 = 7.2 + 0.5pK_a + 0.5 \lg 0.01$$

$$pK_a = 5.4; \quad K_a = 4 \cdot 10^{-6}$$

gives a K_a value that characterizes the nitrosaminic acid. For the values of the acidity constant of the nitrosaminic acid, determined by different methods, to differ on the order of 0.2 is fully permissible. Knowing that the pH value of a 0.01 M aqueous solution of the organic salt formed by the diazo cation and diazo anion is equal to 7.6, and that the acidity constant of the nitrosaminic acid $K_a = 2.5 \times 10^{-6}$, it becomes possible to calculate the basicity constant of the diazohydroxide [8]

$$pH = 0.5pK_W + 0.5pK_a - 0.5pK_b$$

$$7.6 = 0.5 \cdot 14.4 + 0.5 \cdot 5.6 - 0.5pK_b$$

$$pK_b = 4.8; \text{ whence } K_b = 1.6 \cdot 10^{-5}$$

It is easy to see that the basicity constant of the diazohydroxide is nothing else than the second basicity constant of the diazo anion, which can be represented as the quotient of the ionic product of water divided by the first acidity constant of the diazo cation.

$$K_b = K_{b_{II}} = \frac{[RN_2^+][OH^-]}{[RN_2OH]} = \frac{[RN_2^+]K_W}{[RN_2OH][H^+]} = \frac{K_W}{K_{a_I}}$$

From this we obtain the first acidity constant of the diazo cation

$$K_{a_I} = \frac{10^{-14.4}}{10^{-4.8}} = 10^{-9.6} = 2.5 \quad 10^{-10}$$

However, the second acidity constant of the diazo cation (it is the acidity constant of the diazohydroxide) cannot be found as the quotient of the total hydrolysis constant of the diazo cation divided by its first acidity constant, since a tautomeric mixture of the diazohydroxide and nitrosaminic acid is present in the solution. As was indicated above, a similar calculation should unavoidably lead to a constant that characterizes the nitrosaminic acid.

$$K_a = \frac{K}{K_{a_I}} = \frac{10^{-15.2}}{10^{-9.6}} = 10^{-5.6} = 2.5 \cdot 10^{-6}$$

The first basicity constant of the diazo anion can be found in the following manner:

$$K_{b_1} = \frac{[RNHNO][OH^-]}{[RN_2O^-]} = \frac{[RNHNO]K_W}{[RN_2O^-][H^+]} = \frac{K_W}{K_a}$$

$$K_{b_1} = \frac{10^{-14.4}}{10^{-5.6}} = 10^{-8.3} = 1.6 \cdot 10^{-9}$$

As a result, at the present time only the acidity constant of the diazohydroxide remains unknown.

The given calculation again confirmed the validity of the conclusions that we had made on the basis of the results obtained in a potentiometric and spectral investigation of diazo compounds, which conclusions have been reported in earlier communications [1, 6].

SUMMARY

Based on the potentiometric titration of diazo compounds and a study of the electronic absorption spectra of the latter, it is possible to calculate accurately the physicochemical constants of diazo compounds, characterizing their acid-base properties.

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SYNTHESES AND TRANSFORMATIONS OF PYRIMIDINE DERIVATIVES

X. ACTIVITY OF METHYL GROUPS IN 4-METHYLURACIL DERIVATIVES

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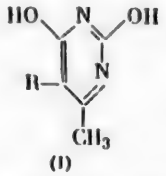
March, 1960
Original article submitted March 25, 1959

In the course of our earlier studies [1] it was established that the activity of the methyl groups in 4-methyluracil (I) derivatives depends on the character of the substituents found in the 5 position. When either a nitro or a diazo group is found in the 5 position, the methyl group proves to be so active that it acquires the ability to react with p-nitrodiazobenzene with the formation of the corresponding azo compounds. On the other hand, it was shown that introducing either a hydroxy or a methyl group in the 5 position of 4-methyluracil is not accompanied by an increase in the activity of the methyl group in the 4 position. Neither 4,5-dimethyluracil nor 4-methyl-5-hydroxyuracil enters into azo-coupling reaction with p-nitrodiazobenzene. A similar result was obtained for the case of 4-methyl-5-bromouracil, where a halogen was introduced in the 5 position. It was shown that 4-methyl-5-bromouracil fails to enter into the azo-coupling reaction with p-nitrodiazobenzene.



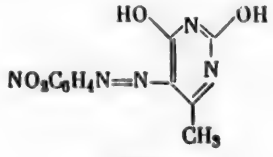
(I)

The present study was undertaken for the purpose of verifying the earlier obtained data on substances similar to the compounds already investigated. As R in the 4-methyluracil molecule we introduced the hydroxymethyl group and iodine.

4-methyl-5-hydroxymethyluracil (II), used at the present time in medical practice under the name of pentoxyl, is characterized by marked instability. This compound decomposes easily when its aqueous solution is heated, with the cleavage of formaldehyde and the formation of 4-methyluracil: (II) $\rightarrow CH_2O$ + (I).

A gradual cleavage of formaldehyde in either alkaline or acid solution also occurs at room temperature. In the dry state 4-methyl-5-hydroxymethyluracil keeps for a long time without noticeable changes.

We were able to show that 4-methyluracil reacts with p-nitrodiazobenzene to yield 4-methyl-5-(p-nitrobenzeneazo)uracil (III). Here the methyl group remains untouched.



(III)

The reaction goes in sodium carbonate solution (either aqueous or alcoholic), but not in glacial acetic acid, as had been shown by us earlier [1]. The reason for this is that in glacial acetic acid solution, in the presence of sodium acetate, the p-nitrodiazobenzene, not reacting with the 4-methyluracil, is converted to 4,4'-dinitrodiazoaminobenzene. •

4-Methyl-5-(p-nitrobenzeneazo)uracil, i.e., an azo dye identical with that obtained by reacting p-nitrodiazobenzene with 4-methyluracil, is formed when 4-methyl-5-hydroxymethyluracil is reacted with p-nitrodiazobenzene in sodium carbonate solution. Consequently, the presence of a hydroxymethyl group in the 5 position failed to exert an activating influence on the methyl group in the 4 position. Also in this case the methyl group failed to enter into reaction with the p-nitrodiazobenzene. The mechanism for the formation of 4-methyl-5-(p-nitrobenzeneazo)uracil from 4-methyl-5-hydroxymethyluracil and p-nitrodiazobenzene reduces to a displacement of the hydroxymethyl group by either the reactant (p-nitrodiazobenzene) or the solvent.

We were able to establish that 4-methyl-5-iodouracil, the same as 4-methyl-5-bromouracil, fails to enter into the azo-coupling reaction with p-nitrodiazobenzene.

4-Methyl-5-iodouracil can be obtained by reacting iodine with 4-methyluracil in alkaline solution. The compound [3] obtained in this manner was characterized as the complex condensation product with composition $C_{10}H_{12}O_5N_2I_2$.

When we repeated the described preparation, it was found that the reaction of iodine with 4-methyluracil in alkaline medium yields a yellow substance with an ill-defined melting point [from the literature [3]: m.p. 180° (with decompn.)]. However, recrystallization of the substance from glacial acetic acid enabled us to obtain it as a colorless crystalline substance with m.p. 238-240°, from its composition corresponding to the formula of 4-methyl-5-iodouracil. Consequently, the reaction of iodine with 4-methyluracil proceeds in the same manner as do other reactions of electrophilic substitution in the uracil series (sulfonation, bromination, nitration, azo-coupling).

The quantitative determination of 4-methyluracil by iodometric titration [4] is based on this reaction. It proved further that the reaction of iodine with 4-methyl-5-hydroxymethyluracil under the same conditions also yields 4-methyl-5-iodouracil. In this case also, the same as in the azo-coupling of 4-methyl-5-hydroxymethyluracil, there occurs a displacement of the hydroxymethyl group by either the reagent (iodine) or the solvent.

EXPERIMENTAL

Preparation of 4-methyl-5-(p-nitrobenzeneazo)uracil. To a solution of 1.1 g of 4-methyluracil in 60 ml of 10% sodium carbonate solution was gradually added, with good stirring, a solution of p-nitrodiazobenzene, prepared from 0.9 g of p-nitroaniline. Here a brick-red precipitate separated, which after 5-6 hr was filtered, washed with hot water, and treated in succession with hot 2% sodium carbonate solution, water, 1% hydrochloric acid solution, and again with water. The substance is insoluble in alkalies, and dissolves with difficulty in water or alcohol when heated. The compound can be recrystallized from acetic acid with large losses. M.p. 208-210° (decompn.).

Found %: N 22.90, 22.94; H_2O 6.30. $C_{11}H_9O_4N_5 \cdot H_2O$. Calculated %: N 23.80; H_2O 6.10.

An azo dye identical with that obtained from 4-methyluracil is formed from 4-methyl-5-hydroxymethyluracil under similar conditions.

Preparation of 4-methyl-5-iodouracil. To a solution of 1.26 g of 4-methyluracil in 15 ml of 10% KOH solution was gradually added, with good stirring, a solution of 2 g of iodine in 10% KOH solution. Acidification with 10% hydrochloric acid solution under cooling gave a yellow precipitate, which was filtered and washed with an aqueous potassium iodide solution and then with water. Two recrystallizations from glacial acetic acid gave the substance as a colorless (or slightly yellow) crystalline compound. The compound can also be recrystallized from a large volume of water. It is insoluble in most organic solvents. M.p. 238-240° (capillary inserted at 235°). The compound melts at 245-248° if heated slowly.

• This same 4,4'-dinitrodiazoaminobenzene was apparently also obtained by A. A. Kharkharov [2], who attempted to azo-couple α-methylpyridine with p-nitrodiazobenzene and erroneously assumed it to be the azo-coupling product.

Found %: N 11.06, 11.09; I 49.8, 50.5. $C_5H_5O_2N_2I$. Calculated %: N 11.11; I 50.30.

The same 4-methyl-5-iodouracil is obtained by reacting iodine with 4-methyl-5-hydroxymethyluracil under the conditions of iodometric titration proposed as a method for the quantitative determination of 4-methyluracil [4].

SUMMARY

1. The reaction of p-nitrodiazobenzene in sodium carbonate solution with either 4-methyluracil or 4-methyl-5-hydroxymethyluracil yields the same azo dye, namely, 4-methyl-5-(p-nitrobenzeneazo)uracil.

2. It was shown that the reaction of iodine in alkaline solution with either 4-methyluracil or 4-methyl-5-hydroxymethyluracil yields the same compound, namely, 4-methyl-5-iodouracil.

3. 4-Methyl-5-iodouracil, the same as 4-methyl-5-bromouracil, does not react with p-nitrodiazobenzene.

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bis-DIALKYLAMINOACETYL DERIVATIVES OF THE BENZIDINE AND 4,4'-DIAMINODIPHENYLETHANE SERIES

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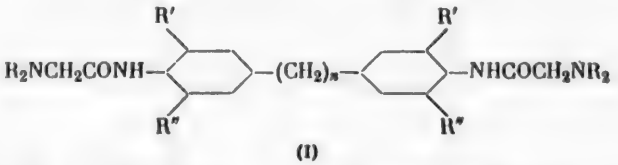
In a search for new local anesthetics and in order to study the relationship between the chemical structure of a compound and its pharmacological action we synthesized a number of bis-dialkylaminoacetyl derivatives of the benzidine and 4,4'-diaminodiphenylethane series, having the general formula (I).



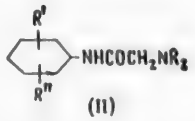
(I)

$n=0$, $R'=R''=H$,
$n=0$, $R'=H$, $R''=CH_3$,
$n=0$, $R'=R''=CH_3$.

$n=2$, $R'=R''=H$.

$NR_2=N(C_2H_5)_2$ or $N<\begin{matrix}CH_2-CH_2\\CH_2-CH_2\end{matrix}>CH_2$.

These compounds are doubled analogs of compounds of the xycaine* series, obtained by us earlier [1], and having the general formula (II).



(II)

From [2] it is known that a "doubling" of the molecule leads to enchanced pharmacological activity.

As the starting amines we took benzidine, o-tolidine, 3,3',5,5'-tetramethylbenzidine and 4,4'-diaminodiphenylethane.

Of all of the isomeric tetramethyl derivatives of benzidine with a symmetrical arrangement of the methyl radicals in both benzene rings, we did not obtain 2,2',3,3'-tetramethyl-4,4'-diaminodiphenyl and 3,3',5,5'-tetramethyl-4,4'-diaminodiphenyl (III, n = 0), the latter needed by us as the starting material for the synthesis of the "doubled" xycaine.

The known 2,2',5,5'- and 2,2',6,6'-tetramethyl derivatives of benzidine were obtained by the benzidine rearrangement of the corresponding hydrazobenzene derivatives [3-5].

This route proved to be unsuitable for the synthesis of the 3,3',5,5'-tetramethyl derivative, since we were unable to obtain the corresponding hydrazo derivative by the reduction of 2-nitro-m-xylene.

*Xycaine is ω-diethylamino-2,6-dimethylacetanilide.

TABLE 1

Expt. No.	n	R′	R″	NR_2	Free base: melting point	found % C	found % H	found % N	calculated % C	calculated % H	calculated % N	Dihydrochloride: melting point	found % N	found % Cl	calculated % N	calculated % Cl	Dimethiodide: melting point	% N found	% N calculated
1	0	H	H	$N(C_2H_5)_2$	135–136°	70.05	8.30	13.59	70.21	8.35	13.64	273° (decompn.)	11.41	14.57	11.58	14.66	248–250°	8.15	8.07
2	0	H	H	NC_5H_{10}	210–212	71.81	7.63	12.80	71.85	7.89	12.89	283–285 "	11.06	13.71	11.04	13.91	245–247 (decompn.)	7.95	7.80
3	0	H	CH_3	$N(C_2H_5)_2$	164–165	71.20	8.75	12.91	71.19	8.73	12.77	277–280	10.72	—	10.95	—	218	7.79	7.75
4	0	H	CH_3	NC_5H_{10}	202–204	72.68	8.35	12.07	72.69	8.28	12.11	257.5–258	10.33	—	10.46	—	235–237	7.51	7.50
5	0	CH_3	CH_3	$N(C_2H_5)_2$	220.5–223	71.99	9.00	12.15	72.06	9.07	12.01	247–251 "	—	13.06	—	13.14	225–230 "	7.24	7.47
6	0	CH_3	CH_3	NC_5H_{10}	205–207	73.30	8.81	11.50	73.43	8.63	11.42	268–271 "	—	12.60	—	12.58	207.5–270	7.39	7.23
7	2	H	H	$N(C_2H_5)_2$	116–118	71.23	8.71	12.58	71.19	8.73	12.77	222–225 "	10.78	—	10.95	—	218.5–220.5	7.50	7.75
8	2	H	H	NC_5H_{10}	164–165	72.66	8.20	12.21	72.69	8.28	12.11	258–262 "	10.38	—	10.46	—	224–227 "	7.56	7.51

We obtained 3,3′,5,5′-tetramethyl-4,4′-diaminodiphenyl by the methylation of o-tolidine hydrochloride with methyl alcohol in a sealed tube at 300-310°. To prove the structure of the compound we prepared the bis-thionyl derivative, which, as is known, is formed only with primary aromatic amines, and the diazo compound, which with H acid gives a violet dye. Quantitive analyses of the synthesized diamine and its bis-thionyl derivative made it possible for us to assume that the obtained diamine is 3,3′,5,5′-tetramethyl-4,4′-diaminodiphenyl.

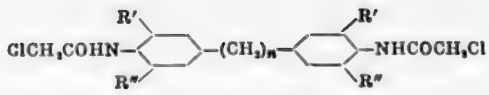
4,4′-Diaminophenylethane was obtained by the reduction of the dinitrodibenzyl with hydrazine hydrate in the presence of Raney nickel in alcohol medium. The 4,4′-dinitrodibenzyl needed for this reaction was synthesized by the procedure described in [6].

The secondary amino groups NR_2 were the diethylamino and piperidine radicals. The obtained free bases were converted to the hydrochlorides and the methiodides. The synthesized compounds are listed in Table 1.

Pharmacological testing* of the compounds revealed that the hydrochlorides of the compounds in the benzidine series have a longer local anesthetic action than do the corresponding compounds in the xycaine series, while the compounds of the diphenylethane series have the same duration of local anesthetic effect as the ω-dialkylamino-4-methylacetanilides. It is interesting to mention that the hydrochlorides of the obtained benzidine derivatives exhibit a much lower toxicity than do the corresponding salts of the aniline derivatives. In reverse, the dimethiodides of the "doubled" compounds are much more toxic than the methiodides of the corresponding aniline derivatives.

*The pharmacological testing was done by P. E. Motovilov and O. G. Plets.

TABLE 2



Expt. No.	n	R'	R"	Melting point	Yield (in %)	Solubility	% N found	% N calculated
1	0	H	H	Begins to decompose at 180°, does not melt.	86	Insoluble in ethanol, methanol, benzene, petroleum ether, and acetone	8.78	8.31
2	0	H	CH_3	Begins to decompose at 260°, does not melt up to 310°.	90	Insoluble in ethanol, methanol benzene, petroleum ether, and acetone	7.80	7.67
3	0	CH_3	CH_3	Does not melt up to 305°.	88	Very difficultly soluble in ethanol	7.24	7.12
4	2	H	H	231.2—233°	93	Difficultly soluble in ethanol	7.61	7.67

EXPERIMENTAL

Preparation of 3,3',5,5'-tetramethylbenzidine. A charge of 1.5 ml of anhydrous methanol and 3.55 g of o-tolidine hydrochloride was placed in a thick-walled ampule. The mixture was heated in the sealed tube for 5 hr at 303-310°. The ampule contents were rinsed out with water, and the solution was then refluxed with carbon for 10 min and filtered. The yellow-green filtrate was then cooled and treated with 20% NaOH solution until alkaline. The obtained precipitate was dried and then recrystallized twice from 50% alcohol. M.p. 164-166°, yield 0.5 g.

Found %: C 79.75; H 8.36; N 11.88. $C_{16}H_{20}N_2$. Calculated %: C 79.95; H 8.39; N 11.65.

Employing a shorter heating time (3 hr) gave a mixture of methylation products, from which we were unable to isolate the pure 3,3',5,5'-tetramethylbenzidine even after repeated recrystallization. Heating for 8 hr at 280-300° resulted in more pronounced tarring.

Preparation of the bis-thionyl derivative of 3,3',5,5'-tetramethylbenzidine. The tetramethylbenzidine (0.1 g) was moistened with 0.5 ml of dry benzene and then 0.99 g of thionyl chloride was added. The mixture was heated under reflux on the boiling water bath for 25 hr. The obtained orange precipitate was filtered, washed first with benzene and then several times with cold water, and dried in a desiccator. M.p. 81-85°.

Found %: N 8.51; S 18.88. $C_{16}H_{16}O_2N_2S_2$. Calculated %: N 8.42; S 19.29.

Preparation of dye. Five milliliters of 1 : 1 hydrochloric acid was added to 0.0243 g of the tetramethylbenzidine. The precipitate failed to dissolve completely even on heating. The cooled, finely crystalline mixture was then treated with 0.0158 g of $NaNO_2$ in 1 ml of water. The obtained yellow solution was neutralized with sodium carbonate, followed by the addition of a solution of 0.0708 g of H acid in 1.5 ml of water, containing a small amount of sodium carbonate. A violet color appeared immediately.

Preparation of 4,4'-diaminodiphenylethane. A charge of 8.17 g of 4,4'-dinitrodibenzyl, 300 ml of alcohol and 20 ml of 90% hydrazine hydrate was placed in a round-bottomed flask fitted with a reflux condenser, mechanical stirrer and thermometer. The mixture was heated to 30° and then about 2 g of Raney nickel was added cautiously with vigorous stirring. Here the temperature should not rise above 60° (external cooling is used if needed). The mixture was heated for 1 hr, cooled, and the nickel was filtered and washed with alcohol. The alcohol was distilled through a Vigreux column, and the residue was allowed to crystallize. The yield was 6.15 g (96.5%). M.p. 136-138° (from 50% alcohol) [7].

Preparation of bis-chloroacetyl derivatives (IV). To a solution of 0.1 g-mole of the amine in 250-300 ml of glacial acetic acid was rapidly added 0.22 g-mole of chloroacetyl chloride, followed by the addition of a solution of 66 g of $CH_3COONa \cdot 3H_2O$ in 280 ml of water. The mixture was stirred for 30 min, and the obtained precipitate was filtered, washed several times with water, and dried. The bis-chloroacetyl derivatives of benzidine and o-tolidine were heated with alcohol, filtered, washed with alcohol and ether, and dried. The bis-chloroacetyl derivatives of the tetramethylbenzidine and 4,4'-diaminodiphenylethane were recrystallized from alcohol. The obtained compounds are listed in Table 2.

Amination of bis-chloroacetyl derivatives. A charge of 0.1 g-mole of the bis-chloroacetyl derivative, 50-70 ml of anhydrous benzene and 0.05 g-mole of either diethylamine or piperidine was placed in a round-bottomed flask fitted with a reflux condenser and calcium chloride tube. The mixture was refluxed in a glycerin bath at 90-100° for 10-12 hr. Then the benzene solution was washed three times with hot water, dried over potassium carbonate, and the benzene distilled off. The residue crystallized. The crystals were dissolved in dilute hydrochloric acid, and the solution was refluxed with carbon and filtered. The filtrate was treated with either concd. ammonia or 30% NaOH solution. The obtained free base was filtered, washed with water, dried, and recrystallized from alcohol, aqueous alcohol or dioxane. Yield 83.5-85.5%.

We used a different method to obtain the bis-dialkylaminoacetyl-3,3',5,5'-tetramethylbenzidine: A mixture of 1.44 g of the bis-chloroacetyl-3,3',5,5'-tetramethylbenzidine and 8 ml of diethylamine or piperidine was heated in a sealed ampule for 7 hr on the boiling water bath and then cooled. The ampule contents were diluted with water, and the precipitate was filtered and washed with water. The precipitate was dissolved in dilute hydrochloric acid (50 ml of water and 5 ml of concd. hydrochloric acid), the solution heated with carbon, filtered and the filtrate made alkaline with either concd. ammonia or 20% NaOH solution. The obtained free base was filtered, washed with water, dried, and recrystallized from 50% alcohol. Yield 80-90%.

Preparation of hydrochlorides. The hydrochlorides of the bis-(diethylaminoacetyl) derivatives of benzidine and o-tolidine were obtained by the addition of the calculated amount of concd. hydrochloric acid to an acetone solution of the free base. The obtained precipitate was filtered, washed with ether, and dried. The hydrochlorides were recrystallized from either methanol or ethanol.

The hydrochlorides of the bis-(piperidinoacetyl) derivatives of benzidine and o-tolidine were obtained in the following manner: The calculated amount of concd. hydrochloric acid was added to the free base and then water was added until all of the substance dissolved when heated. The solution was refluxed with carbon and filtered. A precipitate deposited on cooling; this was filtered, washed with alcohol and ether, and dried in a drying oven at 110-115°. The compounds were recrystallized from water.

The hydrochlorides of the bis-(diethylaminoacetyl) and bis-(piperidinoacetyl) derivatives of 3,3',5,5'-tetramethylbenzidine were obtained by the addition of an anhydrous alcohol solution of the calculated amount of dry HCl to an acetone solution of the free base. The reaction mixture was diluted with dry ether, and the precipitate was filtered, washed with ether, and dried in a drying oven at 110-115°.

The hydrochlorides of the bis-(diethylaminoacetylamino) and bis-(piperidinoacetylamino) derivatives of diphenylethane were obtained in anhydrous alcohol. The calculated amount of 10% alcoholic HCl solution was added to an alcohol solution of the free base. The hydrochloride was precipitated by the addition of dry ether, and the precipitate was filtered, washed with alcohol and ether, and dried.

Preparation of methiodides. The free base was dissolved in the minimum amount of anhydrous acetone, methyl iodide added to the solution, and the whole allowed to stand overnight. The next day dry ether was added to precipitate the product completely; it was then filtered, washed with ether, and dried in a desiccator.

SUMMARY

1. The previously unknown 3,3',5,5'-tetramethylbenzidine was prepared.

2. The following new compounds were prepared: the bis-chloroacetyl derivatives of benzidine, o-tolidine, 3,3',5,5'-tetramethylbenzidine and 4,4'-diaminodiphenylethane, and also bis-(diethylaminoacetyl)benzidine, bis-(piperidinoacetyl)benzidine, bis-(diethylaminoacetyl)-o-tolidine, bis-(piperidinoacetyl)-o-tolidine, bis-(diethylaminoacetyl)-3,3',5,5'-tetramethylbenzidine, bis-(piperidinoacetyl)-3,3',5,5'-tetramethylbenzidine, bis-(diethylaminoacetylamino)diphenylethane, and bis-(piperidinoacetylamino)diphenylethane. The hydrochlorides and methiodides of these compounds were also prepared.

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PREPARATION OF AZELAIC, γ-KETOAZELAIC, AND OTHER ACIDS FROM CYCLOHEXANONE AND ACRYLONITRILE

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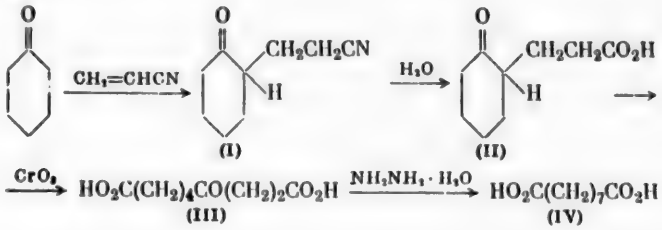
Azelaic acid is of considerable interest as a component of certain forms of polyamide resins which differ in their ability to form very elastic films without addition of a plasticizer, and give alcoholic solutions which do not gelatinize for a long time [1]. Esters of this acid are used in perfumery, and improve the properties of hydrocarbon lubricating oils [2]. The most common methods of its preparation are based on the oxidative destruction of oleic and ricinoleic acids by treatment with chromic acid [3] or potassium permanganate [4], and on the alkali fusion of 9,10-dihydroxystearic acid [5]. Azelaic acid is prepared synthetically by treating the magnesium derivative of 1,7-dibromoheptane with CO_2 [6], by electrolyzing a solution containing the potassium salts of monoethyl suberate and monoethyl malonate [7], by oxidizing 1,11-dodecadiene [8], by hydrolyzing 1,7-dicyanoheptane [9], by acid cleavage of the adduct of dihydroresorcinol and acrylonitrile [10], and by the hydrolysis and subsequent oxidation of 1,1,1,9-tetrachlorononane, which is obtained along with other products through a telomerization reaction [11].

γ-Ketoazelaic acid is prepared by oxidizing the unsaturated acids of certain vegetable oils [22] byoxidizing ethyl β-cyclohexenylpropionate with potassium permanganate [16], and by synthesis with sodiomalonic ester, proceeding from ω-chloro-ε-ketoenanthic acid [23].

The present work was undertaken for the purpose of investigating the possibility of synthesizing azelaic and γ-ketoazelaic acids, proceeding from cyclohexanone and acrylonitrile.

This synthesis was carried out in three steps for γ-ketoazelaic acid and in four steps for azelaic acid, according to the following scheme.

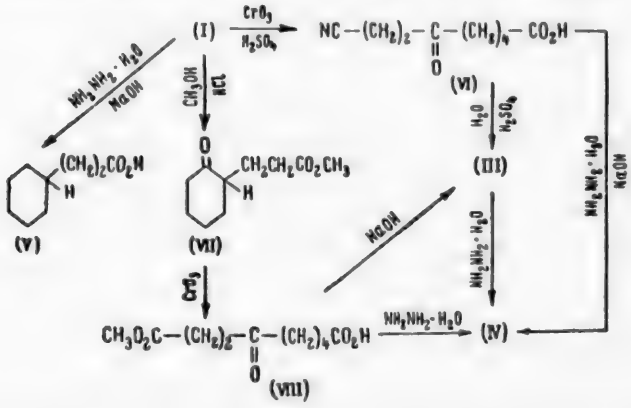


The final yield of γ-ketoazelaic and azelaic acids amounts to 45 and 40%, respectively, reckoned on cyclohexanone, or 50 and 45%, reckoned on acrylonitrile. If the yield in the first step is increased to 90-95%, the over-all yield may be increased correspondingly to 65-70%.

Besides the indicated scheme, we tested another, shorter route of azelaic acid synthesis, in which 2-(β-cyanoethyl)cyclohexanone was directly oxidized by chromic anhydride under mild conditions and the resulting γ-ketoazelaic mononitrile isolated; simultaneously hydrolysis and Wolff-Kizhner reduction of the latter gave azelaic acid in 25% final yield. According to the data obtained, this route is less expedient; this

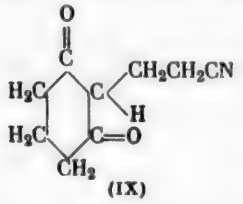
is due not so much to the lower yield of azelaic acid as to insufficient reproducibility of results in the oxidation step, which apparently is explained by the instability of the γ-ketoazelaic mononitrile formed in an acid oxidizing medium. The ketoazelaic acid itself is quite stable under these conditions.

This variant of the synthesis, and also other conversions which the first reaction product (adduct I) underwent in the course of the present investigation, are shown in the following scheme:



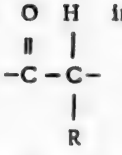
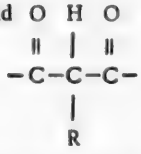
In order to minimize the formation of di- and polycyanoethyl derivatives on cyanoethylation of cyclohexanone, it is recommended [12] that a three- to five-fold molar excess of the latter be taken and that the reaction be carried out at 60-65° in the presence of trimethylbenzylammonium hydroxide catalyst (Trilon "B"). In this case the yield of the monocyanoethyl derivative is 47% [12].

Our experiments showed that when small amounts of aqueous-alcoholic KOH solution are used as catalyst and the spent catalyst is removed by decantation instead of washing, the monocyanoethyl derivative may be obtained in yields of 60-65%, reckoned on cyclohexanone, or 75%, reckoned on acrylonitrile, which is considerably higher than previously recorded yields of this compound [12-14, 18, 20].•



(IX)

The cyanoethyl derivative of 1,3-cyclohexanedione (IX), which is similar in structure to adduct (I), is easily converted to azelaic acid as a result of acid cleavage (according to Stetter [10]) on boiling with a solution of NaOH and hydrazine hydrate in diethylene glycol.

Under the same conditions we obtained not azelaic, but β-cyclohexylpropionic acid from adduct (I); this apparently is explained by the greater stability of the ring in adduct (I) (i.e., the greater stability to hydrolytic cleavage of the bond  in comparison with the bond  in 2-cyanoethyl-1,3-cyclohexanedione).

The ring of adduct (I) and the corresponding acid (II) was broken by oxidation with chromic acid. Besides, acid (II) could be converted to γ-ketoazelaic acid through catalytic oxidation by air in a glacial acetic acid medium by the procedure described for the oxidation of cyclohexanone to adipic acid [24].

EXPERIMENTAL

2-(β-Cyanoethyl)cyclohexanone (I). A solution of 3.0 g of KOH in 2.5 ml of water and 5 ml of methanol was added to 520 g of cyclohexanone. A 48 g quantity of acrylonitrile was added dropwise at an initial temperature of 50°, with stirring, the reaction mixture being periodically cooled so that the temperature was kept between

•According to recent patent data [25], the yield of the monocyanoethyl derivative of cyclohexanone may be increased to 90-95% by carrying out the reaction in the presence of 1-5% amines.

60 and 65°. When all the acrylonitrile had been added, stirring was continued at this temperature for 2 hr more; the mixture was left overnight, and the clear, yellowish solution was decanted from the precipitate of alkaline catalyst. On distillation the fraction with b.p. 80-110° (7-10 ml) was followed by unreacted cyclohexanone, the remainder of which was distilled off in vacuo. The 135-138° (10 mm) fraction, consisting of 2-(β-cyanoethyl) cyclohexanone [13, 14], was collected; it amounted to 90-95 g (56-65%, reckoned on reacted cyclohexanone, or 68-75%, reckoned on the acrylonitrile taken). A dark, solidifying residue (40-50 g)—a mixture of di- and poly-cyanoethyl derivatives—remained in the flask. Freshly distilled mononitrile (I) was a clear, colorless liquid ($n^{20}D$ 1.4766 [19, 20]). On long standing in air it turned yellow. Semicarbazone, m.p. 173-175° (from alcohol).

Found %: C 57.22; H 7.73; N 26.53. $C_{10}H_{16}ON_4$. Calculated %: C 57.63; H 7.72; N 26.90.

β-Cyclohexanonepropionic acid (II). An 84 g quantity of 2-(β-cyanoethyl)cyclohexanone was boiled with 168 ml of hydrochloric acid and 84 ml of water for 3 hr and left overnight, and the hydrolysis product was extracted with ether (10 × 150 ml). The extract was washed with saturated NaCl solution and dried over Na_2SO_4. After distilling off the solvent (in a water-jet pump vacuum toward the end), 82 g (88%) of the crude acid was obtained; the latter was readily soluble in alcohol and ether, and slightly soluble in petroleum ether. B.p. 63-64° (from petroleum ether) [19, 21].

γ-Ketoazelaic acid (III). a) To a solution of 61 g of H_2SO_4 in 100 ml of water at 50°, 43 g of molten β-cyclohexanonepropionic acid was added with vigorous stirring. A solution of 38 g of CrO_3 in 33 ml of H_2SO_4 and 100 ml of water was added dropwise to the mixture during 15 min. The temperature was kept between 50 and 55° by cooling with ice water. Stirring was continued for 2 hr at the same temperature (heating), after which the mixture was left overnight. The partially precipitated acid was separated from the liquid and dissolved in a little warm water; the two solutions were combined and then extracted with ether (10 × 150 ml), and the extract was washed with saturated aqueous NaCl solution and dried over Na_2SO_4. After driving off the ether, 38-39 g (75-77%) of crude γ-ketoazelaic acid with an acid number of 97-98 (calculated 98.8) and m.p. 98-100° was obtained; after recrystallization, m.p. 108.5-109.5° (from $CHCl_3$) [1, 6, 17, 23].

Semicarbazone, m.p. 195-196° [16, 17].

Found %: C 53.21; H 6.85. $C_9H_{14}O_5$. Calculated %: C 53.34; H 6.93.

b) Forty g of β-cyclohexanonepropionic acid was dissolved in 50 g of glacial acetic acid, and 0.1 g of dry manganous acetate was added (the acetate or cobalt naphthenate could be used). The solution was placed in a vertical, glass oxidation apparatus with a porous plate, provided with a reflux condenser, and air was blown through it at a rate of 10-12 liters/hr for 10 hr at 100°. The acid, which precipitated on cooling, was filtered out, washed with water, and dried. There was obtained 35-36 g (70%) of crude γ-ketoazelaic acid contaminated with a certain amount of tars. After three recrystallizations from chloroform, γ-ketoazelaic acid with constants approximating those given above was obtained.

Azelaic acid (IV). To a solution of 33 g of NaOH and 33 ml of 85% hydrazine hydrate in 300 ml of diethylene glycol, 20 g of the ketoazelaic acid was added, and the mixture was refluxed at 140° for 2 hr.

The excess hydrazine hydrate and water were driven off, the temperature was gradually raised to 195-200°, and refluxing was continued at this temperature for 4 hr more. On cooling, 200 ml of water was added, and the mixture was acidified with hydrochloric acid and extracted with ether (10 × 100 ml); the extract was washed with saturated NaCl solution and dried over Na_2SO_4. After distilling off the solvent, 15-16 g (80-85%) of crude azelaic acid, m.p. 106-107° (from water), was obtained. Yield of recrystallized acid 70%.

Found %: C 57.39; H 8.42. $C_9H_{16}O_4$. Calculated %: C 57.42; H 8.56.

β-Cyclohexylpropionic acid (V). Fifteen g of adduct (I) was added to a solution of 20 g of NaOH and 20 ml of 85% hydrazine hydrate in 150 ml of diethylene glycol. The mixture was refluxed for 30 hr at 115° and, when the excess water and hydrazine hydrate had been driven off, 15 hr more at 195°. A 150 ml quantity of water was added to the cooled mass, the mixture was acidified with concentrated hydrochloric acid, and the oil that separated was extracted with ether. After driving off the ether, 15 g of residue was obtained, from which 10 g (60%) of a fraction with b.p. 126-128°(5 mm), $n^{20}D$ 1.4636 was isolated [15].

One g of the acid was boiled with 4 ml of thionyl chloride for 3 hr in a flask with a reflux condenser. The excess thionyl chloride was driven off and the product added dropwise to an aqueous ammonia solution cooled with snow and ice. The precipitated amide melted at 119-120° (from water).

γ-Ketoazelaic mononitrile (VI). Seventy-five g of adduct (I) was added to a solution of 70 ml of conc. H_2SO_4 in 225 ml of water. The resulting emulsion was cooled with a mixture of alcohol and solid carbon dioxide, and a solution of 75 g of CrO_3 in 70 ml of sulfuric acid and 225 ml of H_2O was added dropwise with vigorous stirring, at such a rate that the reaction temperature was kept between 28 and 30°. The solution was left overnight, extracted with ether, washed with saturated NaCl solution, and dried with sodium sulfate. After distilling off the ether, there was obtained 70-75 g (80%) of a quickly solidifying oil, which consisted of crude γ-ketoazelaic mononitrile; the structure of the latter was proved by subsequent conversion to azelaic and γ-ketoazelaic acids.

The crude nitrile was frozen out twice from its solution in 150 ml of ether (first at a temperature of + 5 to 0 and then at - 10°), 30-35 g (33-39%) of pure γ-ketoazelaic mononitrile (ε-keto-ω-cyanocaprylic acid) being obtained in the form of colorless tablets with m.p. 52-54° and an acid number of 54.6 (calculated, 54.64).

Found %: C 58.40; H 7.11; N 7.62. $C_9H_{13}O_3N$. Calculated %: C 58.99; H 7.16; N 7.64.

Semicarbazone of the ketoacid nitrile, m.p. 198° (from alcohol) (decomp.).

Found %: C 49.78; H 6.55; N 23.01. $C_{10}H_{16}O_3N_4$. Calculated %: C 49.99; H 6.70; N 23.32.

Azelaic acid from γ-ketoazelaic mononitrile. Thirty g of the pure nitrile from the preceding experiment was added to a solution of 50 g of NaOH and 30 ml of 85% hydrazine hydrate in 400 ml of diethylene glycol, and the mixture was further treated as in the preceding experiment, 30 g (98%) of crude azelaic acid being obtained. After drying on a porous ceramic plate and recrystallization from water, 20 g of pure azelaic acid, m.p. 105-106°, was obtained. The diamide, prepared as in the preceding experiment, melted at 173° [10].

Found %: C 57.68; H 8.54. $C_9H_{16}O_4$. Calculated %: C 57.42; H 8.56.

Methyl-β-cyclohexanonepropionate (VII). A 205 g quantity of the adduct was dissolved in 225 g of methanol, and gaseous hydrogen chloride was passed through the mixture at the boiling point of the latter for 8 hr. When the ammonium chloride precipitate had been removed and the excess alcohol driven off, the residue was poured into water, extracted with ether, dried with calcium chloride, and distilled.

Two hundred g (80%) of a fraction with b.p. 142-144° (12 mm), $n^{20}D$ 1.4650, was collected.

Monomethyl γ-ketoazelate (VIII). Ninety g of methyl β-cyclohexanonepropionate (VII) was added to a solution of 184 ml of H_2SO_4 in 330 ml of water. The resulting emulsion was strongly cooled and vigorously stirred, and a solution of 110 g of CrO_3 in sulfuric acid (184 ml of H_2SO_4 and 330 ml of water) was added dropwise at 30°. The mass which crystallized on cooling (overnight) was dissolved in water and the oxidized product extracted with ether. The ethereal extract was washed with saturated NaCl solution and dried with Na_2SO_4. After driving off the ether, there remained 58 g of a white mass of monomethyl γ-ketoazelate, m.p. 90-92° (from $CHCl_3$). Semicarbazone, m.p. 191-192° (from aqueous ethanol).

Hydrolysis of the ester with 10% KOH in the cold gave γ-ketoazelaic acid, m.p. 108-110° [16, 17]. The semicarbazone of this acid had m.p. 194-196° (from alcohol) [16, 17].

Azelaic acid from monomethyl γ-ketoazelate. Ten g of the methyl ester was added to a solution of 10 g of NaOH and 10 ml of 85% hydrazine hydrate in 75 ml of diethylene glycol. The mixture was heated at 120° for 2 hr and at 195° for 4 hr, and was further treated as in the preceding experiment. Seven g of a solid precipitate with m.p. 105-106° (from water) was obtained.

SUMMARY

1. The synthesis of azelaic and γ-ketoazelaic acids, proceeding from cyclohexanone and acrylonitrile through 2-(β-cyanoethyl)cyclohexanone and the β-cyclohexanonepropionic acid obtained by its hydrolysis, was carried out.

2. It was shown that in the oxidation of β-cyclohexanonepropionic acid with "chrome mixture," γ-ketoazelaic acid is obtained (in yields up to 75%); the latter is easily converted by Wolff-Kizhner reduction to azelaic acid.

γ-Ketoazelaic acid also may be prepared through the catalytic oxidation of β-cyclohexanonepropionic acid by air in a glacial acetic acid medium.

3. It was found that in a number of cases oxidation of 2-(β-cyanoethyl)cyclohexanone by "chrome mixture" under mild conditions gives γ-ketoazelaic mononitrile, which in turn is easily converted to γ-ketoazelaic or azelaic acid.

4. The conditions of preferential formation (yield 65%) of 2-(β-cyanoethyl)cyclohexanone in the cyanoethylation of cyclohexanone with an alkaline catalyst were found.

5. β-Cyclohexylpropionic acid and methyl β-cyclohexanonepropionate were prepared in the course of the investigation; the latter also was converted to azelaic acid.

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MASS SPECTRA OF VINYLALKYLACETYLENES•

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March, 1960
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A great number of works [1] have been devoted to the mass-spectrometric study of hydrocarbons of various classes. Until now, however, only the lowest member of the homologous series of enyne hydrocarbons—vinylacetylene—has been investigated in this respect.

Recently the authors of the present article briefly characterized the mass spectra of three possible methyl-substituted vinylacetylenes [2]. It was found that the molecular ion has the greatest intensity in all these spectra.

Fragmentary ions are preferentially formed when the molecule is split by breaking a C-H bond. On the curve of distribution of ions with respect to the number of carbon atoms, two maxima (for C_3H_x and C_5H_x ions) are observed for all three isomers. Of the ions formed when the molecule is split by breaking carbon-carbon bonds, the ion of mass 39 is the most intense. Further loss of hydrogen by primary fragmentary ions is characteristic of all isomers.

Taking into account the great importance of mass-spectrometric data in the qualitative and quantitative analysis of hydrocarbons, and also in determining the relation between structure and reactivity, we studied the mass spectra of several members of the homologous series of vinylalkylacetylenes: penten-1-yne-3, hexen-1-yne-3, octen-1-yne-3, and decen-1-yne-3. This hydrocarbon series displays certain peculiarities in chemical behavior, which require theoretical explanation [3].

The work was done with a type MS-1 mass spectrometer and accessories [2, 4]. The spectra obtained for the four vinylalkylacetylenes are given in the table, where the ion-current intensities are expressed in percentages of the maximum peak in the spectra.

As is evident from the data of the table, the maximum in the vinylacetylene spectrum corresponds to the molecular ion. Fragmentary ions resulting from the cleavage of carbon-carbon bonds are not characteristic of vinylacetylene. The most intense fragmentary ions are formed by cleavage of C-H bonds.

Introduction of a methyl radical into a vinylacetylene molecule on the side of the triple bond somewhat decreases the stability of the molecular ion. When the molecule is split by breaking a carbon-carbon bond, intense fragmentary ions appear in the mass spectrum, particularly the ion with mass 39. In the vinylacetylene spectrum the intensity maximum corresponds not to a molecular ion, but to an ion of mass 79, formed as a result of splitting-off of hydrogen from a molecular ion. Fragmentary ions with masses 77, 65, 52, 51, 41, 39, and 27 also are intense. In the vinylbutylacetylene spectrum the fragmentary ion with mass 39 is the most intense. The intensity of the molecular ion is decreased to 22%. Inter alia, fragmentary ions with masses 93, 91, 79, 77, 65, 43, 41, and 27 should be noted. In the vinylhexylacetylene spectrum the ion-current intensity distribution is characterized by an even greater quantity of ions formed by cleavage of carbon-carbon bonds. The 107, 93, 91, 77, 67, 65, 43, 41, and 39 peaks are the most intense. The 79 peak is the maximum.

•Investigations in the field of conjugated systems. CXIV.

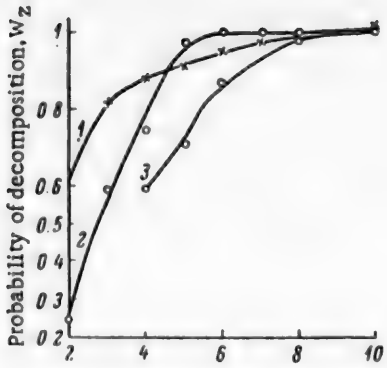


Fig. 1. Probability of decomposition of compounds of various types with respect to the number of carbon atoms in the molecule. 1) Vinylalkylacetylenes; 2) acetylenic hydrocarbons; 3) olefins.

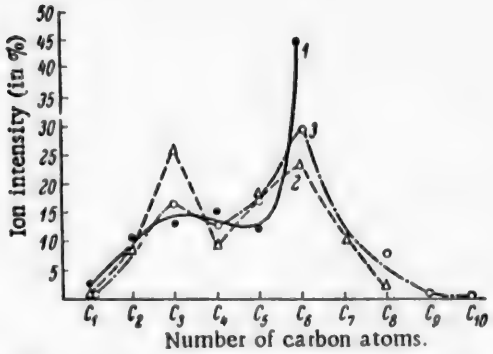


Fig. 2. Distribution of ion intensities in the spectra of vinylalkylacetylenes with respect to the number of carbon atoms. 1) Vinylethylacetylene; 2) vinylbutylacetylene; 3) vinylhexylacetylene.

Thus the following general tendency is observed in the mass spectra of vinylalkylacetylenes: As the size of the alkyl radical increases, the stability of the molecular ion decreases, the intensity of the fragmentary ions increases, and therefore the total intensity of the ions increases.

The intensity of molecular ions, which amounts to 100% in the case of vinylacetylene and vinylmethylacetylene, sharply falls to 1.9% in the case of vinylhexylacetylene. The probability of decomposition $W_z = \frac{\Sigma I_{frag.}}{\Sigma I_{frag.} + \Sigma I_{mol.}}$,* which characterizes the stability of the molecules to electron bombardment, increases with the size of the alkyl radical. For other types of hydrocarbons (paraffins, olefins, acetylenes) the value of W_z also tends toward unity as the molecular weight of the hydrocarbons increases [5].

It is a remarkable fact that, other conditions being equal, the probability of decomposition is determined by the hydrogen content of the molecule and the stability of the molecular ions $C_nH_{2n+2}^+$, $C_nH_{2n}^+$, $C_nH_{2n-2}^+$, and $C_nH_{2n-4}^+$, and varies inversely with the number of hydrogen atoms in the molecule (e.g., at $n = 4$), i.e., an increase in the number of multiple bonds leads to an increase in the stability of the molecular ion to electron bombardment (Fig. 1).

Both the increase in the total intensity of fragmentary ions in the homologous series, and the preferential formation of ions with three and six carbon atoms are characteristic of the vinylacetylenic hydrocarbons investigated (Fig. 2). On a similar ion-intensity distribution curve for paraffin and ethylenic hydrocarbons, there is only one pronounced maximum for C_3H_x ions; in the case of acetylenic and diene hydrocarbons two maxima are observed (Fig. 3).

We believe that these maxima in the intensity distribution curve are due to the preferential formation of ions with conjugated bonds of the types $\overset{+}{C}H_2-\underset{|}{C}=C<$, $\overset{+}{C}H_2-\underset{|}{C}=\underset{|}{C}-\underset{|}{C}=C<$ etc., or rings.

According to current views, the ion-intensity distribution in mass spectra is determined mainly by the energies of the bonds in the molecule. Taking into account this hypothesis, and also the experimentally established stability of carbon-carbon bonds in molecules of vinylacetylene and its methyl derivatives, one may conclude that in molecules of higher vinylacetylenes the γ-carbon-carbon bond (with respect to the conjugated system) is the least stable to electron bombardment. In thermal conversions of unsaturated compounds the β-bond usually proves to be the least stable.

It should be noted that in the spectra of all vinylalkylacetylenes fragmentary ions of the $C_nH_{2n-5}^+$ type have great intensity; examples are the 107, 93, 79, and 65 ions for vinylhexylacetylene, and also ions of the

* $\Sigma I_{frag.}$ is the total intensity of fragmentary ions; $\Sigma I_{mol.}$ is the intensity of molecular ions.

Mass Spectra of Vinylalkylacetylenes

Mass and composition of fragments	$HC\equiv C-CH=CH_2$	$CH_3-C\equiv C-CH=CH_2$	$C_2H_5-C\equiv C-CH=CH_2$	$C_4H_9-C\equiv C-CH=CH_2$	$C_6H_{13}-C\equiv C-CH=CH_2$
	Ion intensities				
12 C^+	1.5	0.9	—	—	—
13 CH^+	1.3	—	—	—	—
14 CH_2^+	1.2	—	—	—	—
15 CH_3^+	0.4	2.0	15.3	9.3	—
25 C_2H^+	3.6	1.6	1.4	—	—
26 $C_2H_2^+$	11.0	3.8	18.1	7.8	—
27 $C_2H_3^+$	2.9	8.3	52.6	78.2	—
28 $C_2H_4^+$	0.5	—	—	—	—
36 C_3	1.5	1.7		—	
37 C_3H^+	5.1	9.5	4.1	—	5.4
38 $C_3H_2^+$	2.2	17.0	9.1	9.7	0.1
39 $C_3H_3^+$	0.8	91.5	59.6	100.0	48.5
40 $C_3H_4^+$	0.6	—	—	23.7	12.2
41 $C_3H_5^+$	—	1.8	15.0	67.3	63.8
42 $C_3H_6^+$	—	—	1.1	3.0	9.4
43 $C_3H_7^+$	—	1.0	1.5	33.3	48.8
48 C_4^+	2.8	—	—	—	—
49 C_4H^+	13.0	4.0	2	—	—
50 $C_4H_2^+$	41.9	10.0	20.6	12.5	7.0
51 $C_4H_3^+$	50.2	17.0	27.7	27.6	19.4
52 $C_4H_4^+$	100.0	—	27.0	16.3	13.2
53 $C_4H_5^+$	4.4	—	16.4	14.8	16.9
54 $C_4H_6^+$	—	—	5.5	2.4	3.7
55 $C_4H_7^+$	—	—	2.9	3.3	23.1
56 $C_4H_8^+$	—	—	2.0	3.6	6.7
57 $C_4H_9^+$	—	—	0.7	—	4.0

(Continuation)

Mass and composition of fragments	$HC\equiv C-CH=CH_2$	$CH_3-C\equiv C-CH=CH_2$	$C_2H_5-C\equiv C-CH=CH_2$	$C_4H_9-C\equiv C-CH=CH_2$	$C_6H_{13}-C\equiv C-CH=CH_2$
	Ion intensities				
60 C_5^+	—	—	0.4	—	—
61 C_5H^+	—	12.0	3.6	—	—
62 $C_5H_2^+$	—	15.0	8.7	6.4	2.9
63 $C_5H_3^+$	—	21.9	18.5	21.4	12.6
64 $C_5H_4^+$	—	—	4.5	7.5	3.1
65 $C_5H_5^+$	—	38.0	42.8	56.6	35.9
66 $C_5H_6^+$	—	100.0	2.0	58.4	28.7
67 $C_5H_7^+$	—	—	0.6	15.7	29.6
68 $C_5H_8^+$	—	—	—	—	4.5
75 $C_6H_3^+$	—	—	5.4	—	—
77 $C_6H_5^+$	—	—	68.1	83.2	45.3
78 $C_6H_6^+$	—	—	18.5	23.4	13.9
79 $C_6H_7^+$	—	—	100.0	85.4	100.0
80 $C_6H_8^+$	—	—	83.2	18.1	32.7
81 $C_6H_9^+$	—	—	4.6	—	5.4
91 $C_7H_7^+$	—	—	—	38.0	36.8
92 $C_7H_8^+$	—	—	—	—	3.4
93 $C_7H_9^+$	—	—	—	64.7	38.6
94 $C_7H_{10}^+$	—	—	—	—	5.8
95 $C_7H_{11}^+$	—	—	—	—	6.7
105 $C_8H_9^+$	—	—	—	—	2.7
106 $C_8H_{10}^+$	—	—	—	—	4.0
107 C_8H_{11}	—	—	—	—	43.9
108 C_8H_{12}	—	—	—	22.5	7.2
121 $C_{10}H$	—	—	—	—	9.9
136 $C_{10}H_{16}$	—	—	—	—	1.9

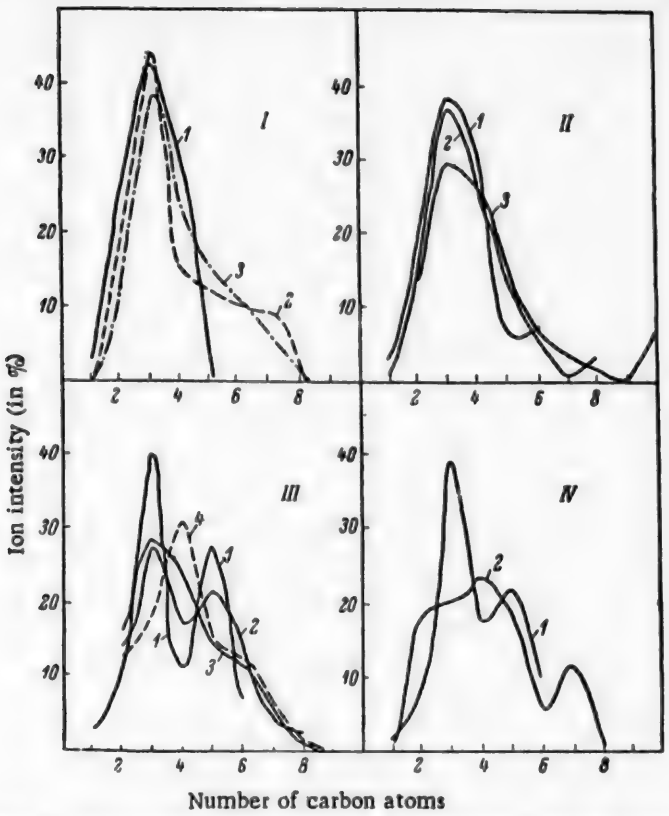


Fig. 3. Distribution of ion intensities with respect to the number of carbon atoms, in the spectra of hydrocarbons of various types. I) Paraffins: 1) n-hexane; 2) n-octane; 3) n-decane. II) Olefins: 1) C_6H_{12}—average of five isomers; 2) C_8H_{16}—average of two isomers; 3) $C_{10}H_{20}$. III) Acetylenes: 1) C_6H_{10}—average of four isomers; 2) C_8H_{14}—average of three isomers; 3) decyne-1; 4) decyne-5. IV) Diolefins: 1) C_6H_{10}—average of two isomers; 2) C_8H_{14}.

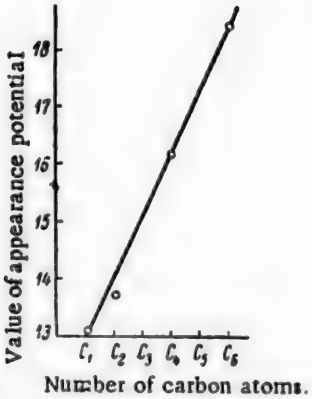


Fig. 4. Effect of the size of the alkyl radical on the appearance potential of the ion with mass 39.

$C_nH_{2n-7}^+$ type, obviously formed from those indicated above with loss of hydrogen, and ions of the $C_nH_{2n-4}^+$ type.

With regard to the mechanism of formation of ions of the type $C_nH_{2n-5}^+$, it may be assumed that they arise as a result of rearrangement with migration of hydrogen; e.g., in the case of the $C_5H_6^+$ ion, according to the scheme:

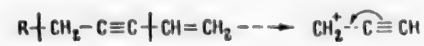
$$CH_3—CH_2—CH_2—CH_2—C\equiv C—CH=CH_2 \longrightarrow$$
$$\longrightarrow CH_3—CH=CH_2 + [CH_3—C\equiv C—CH=CH_2]^+$$

Among other fragmentary ions the ion with mass 39 is remarkable. In the case of vinylmethylacetylene this ion could be formed on splitting of a molecule by breaking a single or double bond. In the interaction between molecules and ionizing electrons both of these routes are possible; however, splitting apparently takes place preferentially by cleavage of the single bond, since the ion with mass 39 is no less intense in the spectrum of isopropenylacetylene (in the case of which the second route of formation of the 39 ion is impossible), and also in the spectra of piperylene and isoprene [1].

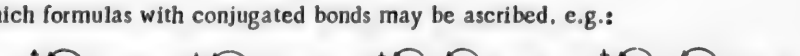
In order to obtain experimental confirmation of the proposed scheme of formation of the 39 ion, we determined the appearance and ionization potentials of this and certain other ion.

In the case of molecular ions the regularity also characteristic of other homologous series of organic compounds was observed. Introduction of a methyl radical somewhat decreased the ionization potential from 9.9 for vinylacetylene to 8.1 for vinylmethylacetylene. Further increase in the size of the radical had practically no effect on the potential.

The appearance potential of the 39 ion varies directly with the size of the alkyl radical (Fig. 4), which possibly indicates a difference in the mechanism of formation of this ion on decomposition of different homologs. It may be assumed that in the case of vinylmethylacetylene the 39 ion is formed by simple cleavage of a C-C bond. In the case of other homologs its formation involves the cleavage of two C-C bonds of different stability and the migration of hydrogen.



ions, to which formulas with conjugated bonds may be ascribed, e.g.:



etc., are remarkably stable. We believe that this regularity is not fortuitous, although it is possible that the arrangement of atoms in the ions does not correspond to that assumed in these formulas.

SUMMARY

1. The mass spectra of several members of the homologous series of vinylalkylacetylenes were investigated.

2. It was shown that as the size of the alkyl radical increases, the stability of the molecular ion decreases and the intensity of the fragmentary ions increases.

3. It was found that among the fragmentary ions formed by breaking carbon-carbon bonds, ions of the types $C_nH_{2n-3}^+$, $C_nH_{2n-5}^+$, $C_nH_{2n-7}^+$, $C_nH_{2n-4}^+$ predominate. Breaking of the γ-bond with respect to the conjugated system is characteristic of higher vinylalkylacetylenes.

4. Certain regularities in the behavior of molecules subjected to electron bombardment, with respect to increase of their unsaturation, were brought out.

5. Certain hypotheses with regard to the mechanism of formation of the most intense ions are set forth.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CXVI. ON THE ADDITION OF LITHIUM DIALKYLAMIDES TO VINYLACETYLENIC HYDROCARBONS •

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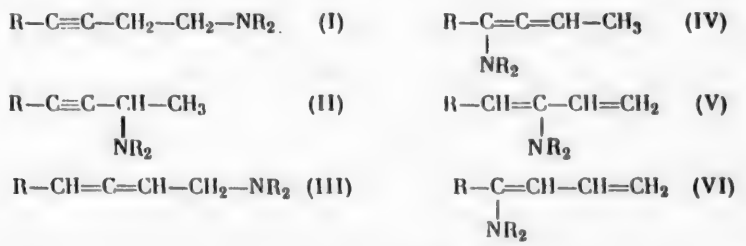
In the literature there is very little material on the chemistry of lithium dialkylamides. These substances were prepared about 25 years ago by treatment of secondary amines with metallic lithium in the presence of organic compounds which could be metalated [1], and were used mainly for the amination or reduction of aromatic compounds [2-5], and also as ester-condensation catalysts [6]. For all these purposes they usually were prepared by treatment of secondary amines with alkyllithiums or aryllithiums.

In a short article we showed that lithium dialkylamides can easily add to conjugated vinylacetylenic hydrocarbons [7]. The reaction goes in the cold and in the absence of any catalyst. At the same time the free amines add, for instance, to vinylacetylene only at elevated temperatures and under pressure [8].

Additional material on the interaction of lithium dialkylamides with vinylacetylenes is given in the present article.

We investigated the addition of lithium dimethyl-, diethyl-, diisopropyl-, and dibutylamides, as well as lithium piperidide and lithium morpholide, to vinyl-, vinylmethyl-, vinylethyl-, and vinylbutylacetylenes. The reaction products were demetalated by treatment with water.

In each case one could expect the formation of the following six amines with three types of multiple bonds (in the scheme R = H or alkyl):



The structure of the amines obtained was proved through infrared spectra, by comparing the constants with literature data (if the expected products were described in the literature), and in three cases by reduction to the corresponding saturated amines and countersynthesis of the latter.

As a result of addition of lithium dialkylamides to vinylacetylene and subsequent treatment of the reaction mixture with water, two amines A and B were usually obtained in a ratio of about 10 : 1 in each case. The

•Enyne compounds, XXXIX.

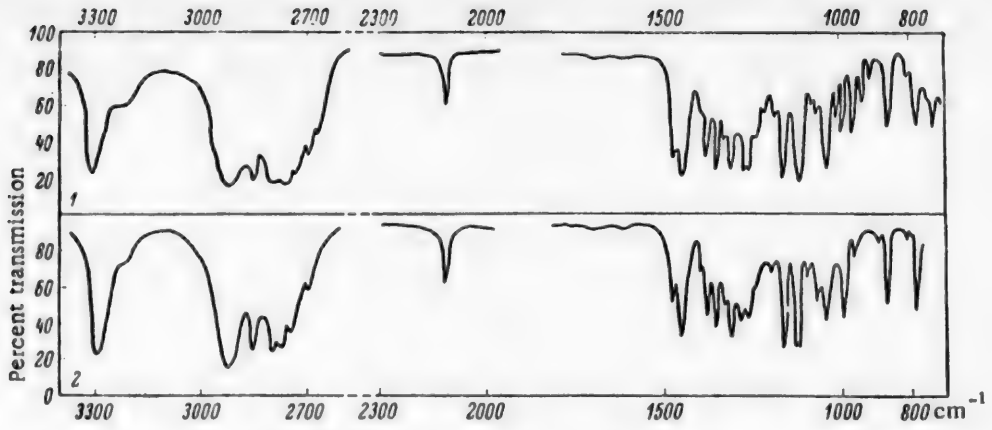


Fig. 1. Infrared transmission spectra. 1) N-Butyn-3-yl-piperidine; 2) the amine $C_{13}H_{19}N$.

main reaction products (amines A) were formed as a result of addition of one molecule of the lithium dialkylamide to one molecule of vinylacetylene. Amines B were adducts of one molecule of the lithium dialkylamide to two molecules of vinylacetylene.

The structure of amines A was established through the infrared spectra and by comparing their constants with the constants of compounds described in the literature.

In the infrared spectra of all adducts there were only bands of valence vibrations of the acetylenic end grouping (3300 and 2120 cm^{-1}); bands of the allenic or 1,3-dienic grouping were absent. Thus formulas (III)-(VI) for amines A were excluded.

1-Dimethylamino- and 1-diethylaminobutynes-3, which are described in the literature, were prepared by addition of lithium dimethyl- and diethylamides to vinylacetylene. Their constants agreed with those given in the literature (Table 1). Isomers with the amino group on the second carbon atom (II) have much lower boiling points and higher refractive indices (2-dimethylaminobutyne-3, b.p. 92-95°; 2-diethylaminobutyne-3, b.p. 128°, $n^{17}D$ 1.4600 [9]). In our case they were not obtained at all.

Products of similar structure were prepared by addition of lithium dibutylamide and lithium piperidide to vinylacetylene. These substances are not described in the literature; in the case of lithium piperidide, however, an isomeric amine with a piperidine group in position 2 (II) is described [9]. It boils much lower (b.p. 58° at 12 mm) than the amine isolated by us.

Thus it was established that lithium dialkylamides add to vinylacetylene with the formation of acetylenic amines of Type (I).

Amines of Type B could be formed by two routes: either by addition of lithium dialkylamides to the previously formed dimer of vinylacetylene, or through a telomerization reaction, i.e., by addition of the original vinylacetylene–lithium dialkylamide adduct to vinylacetylene.

The first hypothesis was excluded, since the dimer of vinylacetylene was not found in the reaction products. The hypothesis that this dimer reacts first and completely with lithium dialkylamides in the presence of an excess of vinylacetylene is unlikely. Hence only the second route remains.

Investigation of the infrared spectra showed that substances of Type B contain an acetylenic end grouping. Multiple bonds of other types were not found. As an example, spectra of amines A and B, obtained from vinyl acetylene and lithium piperidide, are shown in Fig. 1. Intense bands at about 3300 and 2115 cm^{-1} in both spectra correspond to CH and CC valence vibrations of the triple bond. The presence of two acetylenic end groupings in amine B was established by quantitative determination. According to these data, only one route of formation of Type B amines is possible, and their structure is that of 3-dialkylaminomethylheptadiynes-1,6.

$$HC{\equiv}C{-}CH{=}CH_2 \xrightarrow{Li\text{-}NR_2} HC{\equiv}C{-}\underset{\displaystyle Li}{\underset{|}{CH}}{-}CH_2{-}NR_2 \xrightarrow{HC{\equiv}C{-}CH{=}CH_2}$$

$$HC{\equiv}C{-}\underset{\displaystyle Li}{\underset{|}{CH}}{-}CH_2{-}\underset{\displaystyle CH_2{-}NR_2}{\underset{|}{CH}}{-}C{\equiv}CH \xrightarrow{H_2O} HC{\equiv}C{-}CH_2{-}CH_2{-}\underset{\displaystyle CH_2{-}NR_2}{\underset{|}{CH}}{-}C{\equiv}CH$$

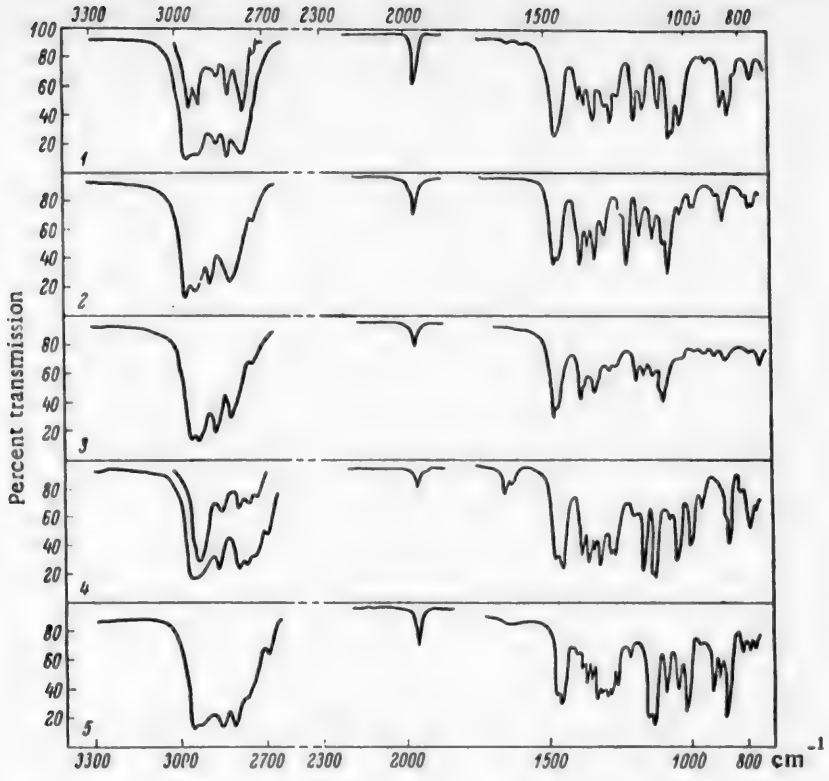


Fig. 2. Infrared transmission spectra. 1) 1-Dimethylaminohexadiene-2,3; 2) 1-diethylaminohexadiene-2,3; 3) 1-dibutylaminohexadiene-2,3; 4) N-hexadien-2,3-yl -piperidine; 5) N-hexadien-2,3-yl-morpholine.

Obviously the given scheme requires further confirmation.

The main products obtained on treatment of vinylmethylacetylene with lithium dialkylamides are the dimer of the hydrocarbon and higher-boiling substances, probably polymers. The yield of amines is of the order of 5-10%.

We proved the structure of the dimer earlier on the basis of data on its hydrogenation to 4-methylnonane, quantitative determination of triple bonds, and investigation of the infrared spectrum (there were found bands characteristic of terminal triple bonds and a conjugated double bond in the grouping -CH = CH-). The substance was assigned the formula of 6-methylnonene-3-dione-1,8.

In order to supplement data published earlier, we prepared an adduct of piperidine to vinylmethylacetylene, together with a dimer and polymers. Like the dimethylamine adduct, the substance has an acetylenic end grouping. In its infrared spectrum there is only a band of valence vibrations of the end triple bond (3300 and 2120 cm^{-1}).

By comparison of infrared spectra it was established that the dimer of vinylmethylacetylene formed in this case is identical with the dimer formed in the reaction with diethylamine.

Repeated experiments on the addition of lithium dibutylamide to vinylmethylacetylene showed that this reaction gives either the previously described allenic amine or a mixture of allenic (III) and acetylenic (I) amines. We were unable to determine just which factors promote the formation of each of these substances. Nevertheless it is obvious that an increase in the particle weight of the radicals in the original amine hinders the formation of amines with an acetylenic end grouping.

We explain the preferential formation of a dimer and polymers in the interaction of lithium dialkylamides with vinylmethylacetylene by the ease of metalation of this substance and the ease of addition of the metalation products to the original hydrocarbon [7].

We proved the structure of the adducts of lithium diethyl- and dibutylamides with vinylethylacetylene earlier by studying their infrared spectra (only bands characteristic of the allenic grouping were found) and by hydrogenating

them to saturated amines, which for comparison were also prepared by another route (from hexyl bromide and diethylamine or dibutylamine).

The amine obtained from the adduct of lithium dimethylamide and vinylethylacetylene, which is described for the first time in the present work, undoubtedly has an allenic grouping. Valence-vibration bands of the acetylenic bond are not found in its spectrum (Fig. 2, Curve 1).

The structure of another amine described for the first time, which was prepared by treating with water the adduct of lithium piperidide and vinylethylacetylene, was proved by means of the infrared spectrum and by exhaustive hydrogenation to hexylpiperidine.

The infrared spectrum of the amine indicated its allenic structure (Fig. 2, Curve 4). However, the spectrum contained weak bands at 1623 and 1645 cm^{-1}, which could belong to double-bond valence vibrations. Therefore the amine obtained by us could contain an admixture of dienic amine (V) or (VI), or an admixture of a dienic amine with a normal chain—a product of allene-diene isomerization of the principal substance. Since exhaustive hydrogenation of the amine gave only n-hexylpiperidine, which was completely identical with the N-hexylpiperidine formed in the reaction of piperidine with n-hexyl bromide, the first hypothesis was rejected.

In the reaction of vinylethylacetylene with lithium morpholide the corresponding amine was obtained in very low yield, and was not isolated in pure form. However, the infrared spectrum of a fraction containing mainly the expected amine was taken, and its structure, also allenic, was established in this way (Fig. 2, Curve 5).

Thus it was proved that lithium dialkylamides, regardless of structure, add to vinylethylacetylene only in the 1,4-position, allenic amines (or products of their allene-diene izomerization) being formed.

Besides adducts of lithium dialkylamides, treatment of vinylethylacetylene with the latter gives very small quantities of a dimer of the original hydrocarbon. We did not isolate it in analytically pure form; however, we investigated the spectrum of a broad fraction (90-100° at 20 mm) containing mainly the dimer, and thus established that it is similar in structure to the dimer of vinylmethylacetylene; i.e., it has terminal acetylenic bonds (bands at 2117 and 2091 cm^{-1}), one of which is conjungated with a double bond (wave-number of the valence vibration 1608 cm^{-1}; that of the deformation vibration, 969 cm^{-1}) in the grouping -CH = CH- (Fig. 3, Curve 2).

Higher homologs of vinylalkylacetylenes do not differ from vinylethylacetylene with respect to the direction of addition of lithium dialkylamides. Thus, for instance, on treatment of vinylbutylacetylene with lithium diethylamide, followed by treatment of the reaction mixture with water, only an allenic amine—diethylaminooctadiene-2,3—was obtained. The structure of the substance was proved through the infrared spectrum.

From the data given it is evident that the addition of lithium dialkylamides to vinylacetylenic hydrocarbons, depending on the structure of the latter, gives two types of amines with the amino group in the same position—acetylenic and allenic amines. Allenic amines obviously are formed as a result of the 1,4-addition of lithium dialkylamides.

In the case of vinylacetylene, acetylenic amines may be obtained either as a result of 1,2-addition or as a result of rearrangement of allenic adducts to acetylenic ones at the instant of reaction (A. E. Favorskii rearrangement). The second route seems more probable, firstly because in the case of vinylmethylacetylene the acetylenic adducts (III) cannot be formed in any other way than by isomerization of allenic adducts, and secondly because alkali-metal amides may cause allene-acetylene isomerization of the hydrocarbons [11]. Moreover, it is generally known that amines have a greater tendency toward A. E. Favorskii rearrangement than hydrocarbons [12, 13]. The cause of rearrangement apparently lies in the fact that metal derivatives of the acetylide type are move stable than lithium alkyls. Thus in the case of vinylacetylene the reaction probably goes according to the scheme:

$$HC\equiv C-CH=CH_2 \xrightarrow{R_2N-Li} H-\underset{\displaystyle Li}{\overset{\displaystyle |}{C}}=C=CH-CH_2-NR_2 \longrightarrow Li-C\equiv C-CH_2-CH_2-NR_2 \xrightarrow{H_2O} HC\equiv C-CH_2-CH_2-NR_2$$

The interaction of lithium dialkylamides with vinylacetylenes may go by a nucleophilic, molecular, or radical mechanism. The order of addition here is the same as in the case of addition of Li alkyls [14] and, probably, as in the case of radical chloroarylation [15]. The nucleophilic attack of the amide ion should be strongly hindered on passing from vinylacetylene to vinylalkylacetylenes. Actually, the latter do not add to diethylamine

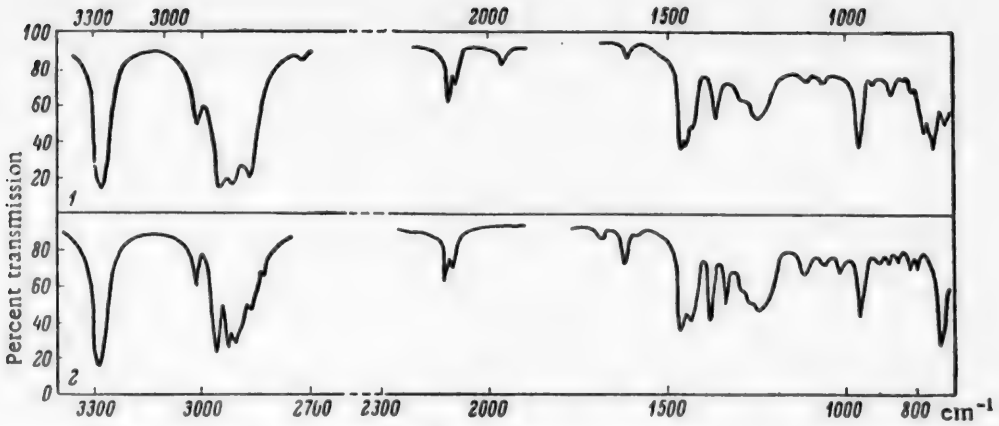


Fig. 3. Infrared transmission spectra. 1) Dimer of vinylethylacetylene; 2) dimer of vinylmethylacetylene.

under those conditions under which vinylacetylene does add.• At the same time, lithium dialkylamides add to vinylalkylacetylenes as readily as to vinylacetylene. These data favor a molecular or radical mechanism.

From Table 1 it is evident that allenic amines are distinguished from acetylenic amines by their considerably greater refractive indices. The values of molar refraction found in both cases are nearly the same as the calculated values; exaltation is not observed.

Comparison of the data for isomeric acetylenic and allenic amines shows that the latter have higher boiling points and specific gravities.

EXPERIMENTAL

The lithium dialkylamides were prepared by treatment of ethereal solutions of ethyllithium or methyllithium (0.5-0.6 mole) with the corresponding secondary amines (0.5-0.7 mole) [2]. When vinylacetylenic hydrocarbons (0.25 mole) were added to these solutions, a vigorous reaction occurred, in which the solution became warmer and changed in color. In those reactions in which the hydrocarbon was vinylmethylacetylene, the reaction mixture turned dirty green; when the hydrocarbon was vinylethylacetylene, the mixture turned brick-red. In the case of vinylacetylene and all lithium dialkylamides except the piperidide color did not appear. On treatment of vinylacetylene with lithium piperidide the reaction mixture first turned red, then bright green, and finally blue.

The reaction was stopped by adding water, usually within 0.5-1 hr after the reaction temperature ceased to rise. In certain experiments with vinylacetylene the reaction mixture was left to stand for 24 hr. In this case we did not observe any appreciable increase in the yields of amines.

The ethereal amine solutions were separated from the water layer, dried over aluminum oxide, and distilled first at ordinary pressure and then in vacuo. The amines were separated from the dimers and polymers by solution in dilute hydrochloric acid (with careful separation of the water layer from the insoluble part) and subsequent precipitation with solid alkali.

Yields of the amines obtained, as well as dimers and polymers, are given in Table 2. Analytical data are given in Table 3.

In the case of vinylacetylene two fractions were always obtained when the amines were fractionally distilled. Thus on fractionation of the amine mixture prepared from lithium piperidide and vinylacetylene [with a Widmer column (20 mm)] the following fractions were obtained: 1st, up to 79.5°, 1.6 g; 2nd, 79.5-80.5°, 19.6 g (22%); 3rd, 80.5-92°, 2.3 g; 4th, 92-93°, 2.6 g (2.5%); residue, 1 g.

• This question was investigated in our laboratory by I. A. Maretina.

TABLE 1

Substance	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated
$HC\equiv C-CH_2-CH_2N(CH_3)_2$	107° (758) 107 (760)	0.7892 0.7896	1.4290 1.4290 [9]	31.74	31.85
$HC\equiv C-CH_2-CH_2N(C_2H_5)_2$	143—143.5 (765) 85 (110) 85 (110)	0.8031	1.4388 1.4390 [10]**	40.99	41.08
$HC\equiv C-CH_2-CH_2N(C_4H_9)_2$ *	104—106 (20)	0.8098	1.4442	59.50	58.55
$HC\equiv C-CH_2-CH_2N(CH_2)_5$	80 (20)	0.8837	1.4740	43.64	43.50
$HC\equiv C-CH_2-CH_2-CH_2N(C_2H_5)_2$	60—61.5 (20) 76 (40) 76 (40)	0.7901	1.4378 1.4380 [9]***	46.24	45.70
$HC\equiv C-CH_2-CH_2-CH_2N(CH_2)_5$	90 (20)	0.8764	1.4712	48.25	48.12
$C_2H_5-CH=C=CH-CH_2N(CH_3)_2$	59—60 (20)	0.7964	1.4510	42.33	42.15
$C_2H_5-CH=C=CH-CH_2N(C_2H_5)_2$	85—86 (20)	0.8111	1.4554	51.30	51.39
$C_2H_5-CH=C=CH-CH_2N(C_4H_9)_2$	136—136.5 (20)	0.8150	1.4558	69.80	69.86
$C_2H_5-CH=C=CH-CH_2N(CH_2)_5$	113—114 (20)	0.8800	1.4800	53.35	52.99
$C_4H_9-CH=C=CH-CH_2N(C_2H_5)_2$	114—115 (20)	0.8148	1.4570	60.16	60.62

* The amine was not quite pure.

** At 18°.

*** At 22°.

TABLE 2

Original hydrocarbon	Lithium dialkylamide	Reaction time (hr)	Yield of amines (in %)	Yield of dimers and polymers (in %)
$HC\equiv C-CH=CH_2$	$Li-N(CH_3)_2$	24	25	None
	$Li-N(C_2H_5)_2$	24	20	None
	$Li-N(C_4H_9)_2$	24	10	None
	$Li-N(CH_2)_5$	3	30	None
$CH_3-C\equiv C-CH=CH_2$	$Li-N(C_2H_5)_2$	24	5	60
	$Li-N(C_4H_9)_2$	1.5	4	50
	$Li-N(CH_2)_5$	1.5	9	56
$C_2H_5-C\equiv C-CH=CH_2$	$Li-N(CH_3)_2$	1.0	40	10
	$Li-N(C_2H_5)_2$	1.5	45	10
	$Li-N(C_4H_9)_2$	1.5	55	Not determined
	$Li-N(CH_2)_5$	1.5	50	
	$Li-N(CH_2)_4O$	24	10	
$C_4H_9-C\equiv C-CH=CH_2$	$Li-N(C_2H_5)_2$	1.5	40	5

On redistillation the 79.5-80.5° (20 mm) fraction boiled at the same pressure, at constant temperature (80°). Constants and analytical data for this fraction are given in Tables 1 and 3.

The amine with b.p. 92-93° (20 mm) had d^{20}_4 0.9032, $n^{20}D$ 1.4800. MR_D 60.06; calc. 59.97.

Found %: C 82.73, 82.93; H 10.08, 10.26; N 7.63, 7.65. M 188.2, 189.8. Number of active H 1.83, 1.87. $C_{13}H_{19}N$. Calculated %: C 82.48; H 10.01; N 7.40. M 189.3. Number of active H 2.

The amines obtained from vinylethylacetylene and three lithium dialkylamides—lithium diethylamide, lithium dibutylamide, and lithium piperidide—were hydrogenated. Hydrogenation data for the first two amides were given earlier [7].

TABLE 3

Substance	Found (%)			Calculated (%)		
	C	H	N	C	H	N
$HC\equiv C-CH_2-CH_2N(C_4H_9)$	80.36, 80.38	13.06, 12.95	8.11	79.49	12.78	7.73
$HC\equiv C-CH_2-CH_2N(CH_2)_5$	78.50, 79.05	10.85, 11.46	10.09, 10.12	78.77	11.02	10.21
$CH_3-CH=C=CH-CH_2N(C_4H_9)_2$	79.71, 79.75	12.94, 13.07	7.52	79.93	12.90	7.17
$HC\equiv C-CH_2-CH_2-CH_2N(CH_2)_5$	79.73, 79.10	11.37, 11.33	9.76, 9.86	79.41	11.33	9.26
$C_2H_5-CH=C=CH-CH_2N(CH_3)_2$	76.36, 76.80	12.12, 12.15	11.11, 11.75	76.73	12.08	11.19
$C_2H_5-CH=C=CH-CH_2N(CH_2)_5$	79.70, 80.27	11.69, 11.84		79.94	11.59	
$C_4H_9-CH=C=CH-CH_2N(C_2H_5)_2$	79.25	12.67	7.52	79.49	12.78	7.73

On exhaustive hydrogenation of the latter amine (piperidinohexadiene-2,3) on colloidal palladium, N-hexylpiperidine was obtained in 91% yield.

B.p. 103-104° (20 mm), d^{20}_4 0.8292, $n^{20}D$ 1.4522, MR_D 55.10; calc. 54.74.

Found %: C 78.01, 77.92; H 13.75, 13.78; N 8.32, 8.20. $C_{11}H_{23}N$. Calculated %: C 78.03; H 13.70; N 8.27.

For comparison this same amine was prepared by brief heating of piperidine with hexyl bromide at 100°. The reaction mixture was disolved in dilute hydrochloric acid. The amine was liberated from the salt by means of solid NaOH.

B.p. 103-104° (20 mm), d^{20}_4 0.8284, $n^{20}D$ 1.4518.

The infrared spectrum of this amine was identical with that of the sample described above.

In two experiments on the interaction of lithium dibutylamide with vinylmethylacetylene, amines having different constants were obtained. The infrared spectrum of the first sample, described earlier, contained only the band of the allenic grouping (1965 cm^{-1}). The infrared spectrum of the second sample contained bands (2121 and 3307 cm^{-1}) characteristic of the allenic and terminal acetylenic groupings.

B.p. 120-124° (20 mm), d^{20}_4 0.8130, $n^{20}D$ 1.4498.

Lithium diisopropylamide did not add to vinylethylacetylene under the conditions which we used.

In the reaction of vinylethylacetylene with lithium morpholide,• a substance with b.p. 120° (20 mm), d^{20}_4 0.9259, $n^{20}D$ 1.4780 was obtained in about 10% yield. The analytical data were unsatisfactory. The spectrum of the substance is shown in Fig. 2, Curve 5.

The infrared spectra were taken with an IKS-14 spectrophotometer provided with LiF and NaCl prisms; the layer thickness was 0.032 mm.•• Data for allenic and certain acetylenic amines are given in Figs. 1 and 2. The infrared spectra of acetylenic amines are discussed in greater detail in another article [16].

SUMMARY

1. The direction of addition of lithium dialkylamides, prepared from dimethyl-, diethyl-, and dibutylamines and piperidine, to vinylacetylenic hydrocarbons (vinylacetylene, vinylmethylacetylene, vinylethylacetylene, and vinylbutylacetylene) was investigated.

• When morpholine was treated with methyllithium in ethereal solution, lithium morpholide separated in the form of a white, crystalline precipitate.

•• T.V. Yakovlev took part in the investigation of the infrared spectra; for this the authors express to him their thanks.

2. It was shown that in the case of vinylacetylene, treatment of the reaction products with water gives two types of acetylenic amines: $HC \equiv C-CH_2-CH_2NR_2$ and (in low yield) probably $HC \equiv C-CH_2-CH_2-\underset{\displaystyle CH_2NR_2}{\underset{|}{CH}}-C \equiv CH$.

3. Vinylmethylacetylene gives mainly the dimer and polymers on treatment with lithium dialkylamides. The structure of the amines depends on the nature of the added lithium dialkylamides: In the case of lithium dibutylamide the main product is the allenic amine; in all other cases, only the acetylenic amines $HC \equiv C-CH_2-CH_2-CH_2NR_2$ are obtained.

4. On addition of lithium dialkylamides to vinylethyl- and vinylbutylacetylenes, the allenic amines $R-CH=C=CH-CH_2NR_2$ and a small amount of dimers and polymers were obtained.

5. Hypotheses on the mechanism of formation of all products on treatment of differently constructed vinylacetylenic hydrocarbons with lithium dialkylamides are advanced.

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ON THE ADDITION OF TRICHLOROSILANE TO TRIALKYL (PHENYL, CHLORO) ALLYLSILANES

CERTAIN SILICOHYDROCARBONS OF THE DISILYLPROPANE SERIES

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A new method of preparation of organosilicon compounds by addition of hydride silanes to various unsaturated hydrocarbons is described in the literature [1]. It was shown that compounds containing a carbon bridge between the silicon atoms could be obtained through the interaction of trichlorosilane with acetylene, vinyltrichlorosilane, and allyltrichlorosilane [2, 3].

Later the interaction of trichlorosilane with trialkylvinylsilanes and dialkyldivinylsilanes was investigated [4]. Acetyl peroxide, benzoyl peroxide, and ultraviolet radiation were used as initiators of the reaction in the above-mentioned works.

In recent years works have appeared in which platinum on charcoal, chloroplatinic acid [5-10], organic bases [11-14], and other materials [8, 10, 15] were used as catalysts for the addition of hydride silanes to unsaturated compounds.

In the literature there are statements [13, 14, 16] to the effect that the addition of hydride silanes to unsaturated compounds may go either according to Markovnikov's rule or contrary to it, depending on the catalyst used. On addition of trichlorosilane to vinyltrichlorosilane in the presence of $NiCl_2 \cdot 4C_5H_5N$, two isomers were isolated [14].

$$CH_2{=}CHSiCl_3 + HSiCl_3 \begin{cases} \nearrow Cl_3SiCH_2CH_2SiCl_3 \\ \searrow Cl_3SiCHSiCl_3 \\ \qquad\quad | \\ \qquad\quad CH_3 \end{cases}$$

A similar observation was made in a study of the addition of methyldichlorosilane to butyl acrylate in the presence of platinized charcoal [16].

In the preceding article [17] we described the addition of hydride silanes to monoallyl derivatives of silicon. It was of interest to us to study the interaction of trichlorosilane with various monoallyl derivatives of silicon in the presence of benzoyl peroxide and chloroplatinic acid, to prepare certain hexaalkyl(phenyl) derivatives of disilylpropane from the addition products, and also to determine the structure of the compounds obtained, through infrared spectroscopy.

On comparison of the yields of addition products of trichlorosilane with monoallyl derivatives of silicon in the presence of benzoyl peroxide and chloroplatinic acid (see Table 2) it is evident that chloroplatinic acid is a more active catalyst than benzoyl peroxide. Thus trimethylallylsilane and triethylallylsilane practically did not react with trichlorosilane in the presence of benzoyl peroxide on heating for 25 hr at 45-65°. Addition

products of trichlorosilane with trimethylallylsilane and triethylallylsilane in the presence of benzoyl peroxide were obtained only in an autoclave at 100-120° and 300 atm pressure, the yields even in this case being very low – 2.5 and 10%, respectively. In the presence of chloroplatinic acid the yields were 50%. On addition of trichlorosilane to tripropylallylsilane, tributylallylsilane, triphenylallylsilane, and trichloroallylsilane in the presence of benzoyl peroxide the yields correspondingly increased from 3.4 to 62%. We observed a similar regularity in the presence of chloroplatinic acid.

The investigation showed that the activity of the double bond in monoallyl derivatives of silicon with respect to addition reactions depends on the nature of the atoms and groups attached to the silicon atom. As the organic radicals increase in size in trialkylallylsilanes, the activity of the double bond in the allyl radical increases. When the alkyl radicals in trialkylallylsilanes are replaced by electronegative substituents (phenyl or chlorine), the double bond in the allyl radical becomes even more active.

A series of hexaalkyl(phenyl) derivatives of disilylpropane were synthesized through the interaction of chloro derivatives of disilylpropane (obtained by addition of trichlorosilane to monoallyl derivatives of silicon) with alkyllithiums; their physicochemical properties and analyses are given in Table 3.

It was established by means of the infrared spectra* of hexaalkyl(phenyl) derivatives of disilylpropane, that the addition of trichlorosilane to trialkyl(phenyl, chloro)allylsilanes goes contrary to Markovnikov's rule.

$$R_3SiCH_2CH{=}CH_2 + HSiCl_3 \longrightarrow R_3SiCH_2CH_2CH_2SiCl_3$$

$R = CH_3$, C_2H_5, C_3H_7, C_4H_9, C_6H_5, Cl.

EXPERIMENTAL

I. Preparation of Trialkyl(phenyl, chloro)allylsilanes

Trialkyl(phenyl, chloro)allylsilanes were prepared by organomagnesium synthesis, and corresponded in their properties to literature data (Table 1).

1. Trimethylallylsilane. A 48.6 g quantity of magnesium, 181.5 g of allyl bromide, and 108.5 g of trimethylchlorosilane gave 65.0 g of trimethylallylsilane.

2. Triethylallylsilane. A 24.3 g quantity of magnesium, 100 g of allyl bromide, and 80 g of triethylchlorosilane gave 61.2 g of triethylallylsilane.

3. Tripropylallylsilane. A 24.3 g quantity of magnesium, 100 g of allyl bromide, and 96.2 g of tripropylchlorosilane gave 73.2 g of tripropylallylsilane.

4. Tributylallylsilane. A 24.3 g quantity of magnesium, 80.0 of allyl bromide, and 70.4 of tributylchlorosilane gave 54.6 of tributylallylsilane.

5. Triphenylallylsilane. A 24.3 g quantity of magnesium, 60.5 g of allyl bromide, and 57 g of triphenylchlorosilane gave 29.6 g of triphenylallylsilane.

6. Phenyldimethylallylsilane. Thirty g of magnesium, 121.0 of allyl bromide, and 60.0 g of phenyldimethylchlorosilane gave 38.0 g of phenyldimethylallylsilane.

7. Trichloroallylsilane. Thirty g of magnesium, 190 g of allyl bromide, and 340 g of silicon tetrachloride gave 53.5 g of trichloroallylsilane.

Found %: Cl 60.38, 60.68. $C_3H_5Cl_3Si$. Calculated %: Cl 60.69.

II. Addition of Trichlorosilane to Trialkyl(phenyl, chloro)allylsilanes

The corresponding monoallyl derivative of silicon and the catalyst were put into a three-neck flask provided with a stirrer, reflux condenser, and dropping funnel, and trichlorosilane was slowly introduced with stirring. When chloroplatinic acid was employed, it was used in the form of a 0.1 N solution of $H_2PtCl_6 \cdot 6H_2O$ in propanol-2.

*The spectral investigation was carried out by Yu. P. Egorov.

TABLE 1

Trialkyl(aryl)allylsilanes

No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D calculated	MR_D found	Yield (in %)
1	$(CH_3)_3SiCH_2CH=CH_2$	85.5—87° (756)	1.4074	0.7202	39.25	39.00	57.0
2	$(C_2H_5)_3SiCH_2CH=CH_2$	170—171.5 (748)	1.4441	0.7868	52.78	52.76	73.8
3	$(C_3H_7)_3SiCH_2CH=CH_2$	216—217 (748)	1.4490	0.7950	67.03	66.94	74.0
4	$(C_4H_9)_3SiCH_2CH=CH_2$	145—146 (12)	1.4531	0.8030	80.68	80.79	77.6
5	$(C_6H_5)_3SiCH_2CH=CH_2$	190 (5). M.p. 90°	—	—	—	—	52.0
6	$(C_6H_5)(CH_3)_2SiCH_2CH=CH_2$	90 (4)	1.5069	0.8915	59.07	58.76	61.7
7	$Cl_3SiCH_2CH=CH_2$	116—118 (756)	1.4461	1.2286	37.96	38.14	20.3

TABLE 2

Trialkyl(aryl)trichlorodisilylpropanes

No.	Compound	Boiling point (pressure in mm)	% Cl calculated	% Cl found	Yield (in %) benzoyl peroxide	Yield (in %) chloroplatinic acid $H_2PtCl_6 \cdot 6H_2O$
1	$(CH_3)_3SiCH_2CH_2CH_2SiCl_3$	187—189° (742)	42.63	42.38 42.53	2.5 *	50.0
2	$(C_2H_5)_3SiCH_2CH_2CH_2SiCl_3$	126—127 (5)	36.48	36.26 36.41	10.0 *	51.2
3	$(C_3H_7)_3SiCH_2CH_2CH_2SiCl_3$	167—169 (12)	31.89	31.89 32.17	3.4	59.2
4	$(C_4H_9)_3SiCH_2CH_2CH_2SiCl_3$	176—178 (4)	28.32	28.25 27.88	13.2	61.9
5	$C_6H_5)_3SiCH_2CH_2CH_2SiCl_3$	237—239 (2)	24.59	24.46 24.20	29.1	68.3
6	$(CH_3)_2C_6H_5)SiCH_2CH_2CH_2SiCl_3$	153—155 (7)	34.19	33.85 33.79	22.0	57.2
7	$Cl_3SiCH_2CH_2CH_2SiCl_2$	116.5—118 (5)	68.45	68.76 68.94	62.2	80.8

*Yield obtained at 100-120° and 300 atm pressure.

When benzoyl peroxide was employed as catalyst, the reaction mass was heated for 18 hr at 45-65°; in the presence of $H_2PtCl_6 \cdot 6H_2O$, the reaction mixture was heated for 10 hr at 50° and then for 2 hr at 80° (see Table 2).

We also carried out experiments on the addition of trichlorosilane to trimethylallylsilane and triethylallylsilane in the presence of benzoyl peroxide in an autoclave.

1. Trimethyltrichlorodisilylpropane. a) A mixture of 57 g of trimethylallylsilane, 100 g of trichlorosilane, and 5 g of benzoyl peroxide was heated for 25 hr at 45-65°. Practically no addition product was obtained.

b) A mixture of 66 g of trimethylallylsilane, 487 g of trichlorosilane, and 5 g of benzoyl peroxide was heated for 18 hr in an 0.8-liter steel autoclave at 100-120° and 300 atm pressure. There was obtained 2.0 g (2.5%).

c) Fifty g of trimethylallylsilane and 65 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 38.2 g (50%).

TABLE 3

Hexaalkyl(phenyl) Derivatives of Disilylpropane

No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found (%) C	Found (%) H	Calculated (%) C	Calculated (%) H
1	$(CH_3)_3SiCH_2CH_2CH_2Si(CH_3)_3$	167—169° (748)	1.4218	0.7584	63.09	63.06	57.22, 57.51	12.74, 12.72	57.37	12.84
2	$(C_2H_5)_3SiCH_2CH_2CH_2Si(C_2H_5)_3$	140—141 (3)	1.4572	0.8253	89.98	90.12	66.10, 66.23	13.35, 13.53	66.10	13.31
3	$(C_3H_7)_3SiCH_2CH_2CH_2Si(C_3H_7)_3$	182—183 (4)	1.4590	0.8245	118.25	118.62	70.77, 70.81	13.62, 13.60	70.70	13.56
4	$(C_4H_9)_3SiCH_2CH_2CH_2Si(C_4H_9)_3$	216—218 (3.5)	1.4624	0.8304	146.06	145.92	73.55, 73.59	13.51, 13.60	73.55	13.72
5	$(C_6H_5)_3SiCH_2CH_2CH_2Si(C_6H_5)_3$	M.p. 120—121°	—	—	—	—	83.63, 83.65	6.44, 6.30	83.52	6.47
6	$(CH_3)_2(C_6H_5)SiCH_2CH_2CH_2Si(CH_3)_2(C_6H_5)$	116—118 (8)	1.4430	0.7980	76.58	76.95	62.76, 62.67	13.26, 13.21	62.53	13.11
7	$(CH_3)(C_6H_5)SiCH_2CH_2CH_2Si(CH_3)(C_6H_5)$	147—148 (8)	1.4461	0.8033	90.50	90.84	66.09, 66.18	13.37, 13.42	66.09	13.31
8	$(CH_3)_2(C_6H_5)SiCH_2CH_2CH_2Si(CH_3)_2(C_6H_5)$	170—172 (8)	1.4499	0.8102	104.35	104.39	68.72, 68.86	13.52, 13.42	68.70	13.45
9	$(CH_3)_3SiCH_2CH_2CH_2Si(C_6H_5)_3$	219—221 (4) M.p. 71—72°	—	—	—	—	76.85, 76.84	7.80, 7.90	76.94	8.07

2. Triethyltrichlorodisilylpropane. a) A mixture of 39 g of triethylallylsilane, 50 g of trichlorosilane, and 5 g of benzoyl peroxide was heated for 25 hr at 45-65°. Practically no addition product was obtained.

b) A mixture of 46 g of triethylallylsilane, 270 g of trichlorosilane, and 5 g of benzoyl peroxide was heated for 18 hr in an 0.8-liter steel autoclave at 100-120° and 300 atm pressure. There was obtained 8.5 g (10%).

c) Forty-two g of triethylallylsilane and 50 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 40.1 g (51.2%).

3. Tripropyltrichlorodisilylpropane. a) Sixty g of tripropylallylsilane, 122 g of trichlorosilane, and 5 g of benzoyl peroxide gave 3.5 g (3.4%).

b) Thirty-two g of tripropylallylsilane and 40 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 31.5 g (59.2%).

4. Tributyltrichlorodisilylpropane. a) Forty-seven g of tributylallylsilane, 82 g of trichlorosilane, and 5 g of benzoyl peroxide gave 10 g (13.2%).

b) Forty g of tributylallylsilane and 40 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 27.3 g (61.9%).

5. Triphenyltrichlorodisilylpropane. Ten g of triphenylallylsilane, 15 g of trichlorosilane, and 3 g of benzoyl peroxide gave 4.1 g (29.1%).

b) Twenty-one g of triphenylallylsilane and 20 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 20.7 g (68.3%).

6. Phenyldimethyltrichlorodisilylpropane. a) Thirty-five g of phenyldimethylallylsilane, 55 g of trichlorosilane, and 4 g of benzoyl peroxide gave 13.6 g (22%) of phenyldimethyltrichlorodisilylpropane.

b) Thirty g of phenyldimethylallylsilane and 34 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 30.2 g (57.2%) of phenyldimethyltrichlorodisilylpropane.

7. Hexachlorodisilylpropane. a) Ten g of trichloroallylsilane, 20 g of trichlorosilane, and 0.5 g of benzoyl peroxide gave 11.2 g (62.2%).

b) Thirty-six g of trichloroallylsilane and 40 g of trichlorosilane in the presence of 1 ml of $H_2PtCl_6 \cdot 6H_2O$ solution gave 51.0 g (80%).

III. Preparation of Hexaalkyl(phenyl) Derivatives of Disilylpropane (Table 3)

1. Hexamethyldisilylpropane. Ten g of lithium, 100 g of methyl iodide, and 30 g of trimethyltrichlorodisilylpropane gave 18.3 g (80.5%).

2. Hexaethyldisilylpropane. A 7.8 g quantity of lithium, 60 g of ethyl bromide, and 30 g of triethyltrichlorodisilylpropane gave 21.2 g (76.2%).

3. Hexapropyldisilylpropane. A 7.4 g quantity of lithium, 65 g of propyl bromide, and 30 g of tripropyltrichlorodisilylpropane gave 27.0 g (87.0%).

4. Hexabutyldisilylpropane. A 4.5 g quantity of lithium, 45 g of butyl bromide, and 27.3 g of tributyltrichlorodisilylpropane gave 24.2 g (76.3%).

5. Hexaphenyldisilylpropane. A 2.8 g quantity of lithium, 31.4 g of bromobenzene, and 15 g of triphenyltrichlorodisilylpropane gave 9.5 g (50%).

6. Trimethyltriethyldisilylpropane. A 7.0 g quantity of lithium, 55 g of ethyl bromide, and 20 g of trimethyltrichlorodisilylpropane gave 13.6 g (73.7%).

7. Trimethyltripropyldisilylpropane. A 5.6 g quantity of lithium, 49.2 g of propyl bromide, and 20 g of trimethyltrichlorodisilylpropane gave 15.8 g (72.4%).

8. Trimethyltributyldisilylpropane. A 5.6 g quantity of lithium, 55 g of butyl bromide, and 20 g of trimethyltrichlorodisilylpropane gave 18.4 g (73.0%).

9. Trimethyltriphenyldisilylpropane. A 5.6 g quantity of lithium, 63 g of bromobenzene, and 20 g of trimethyltrichlorodisilylpropane gave 23.3 g (77.9%).

SUMMARY

1. The addition of trichlorosilane to trialkyl(phenyl, chloro)allylsilanes in the presence of benzoyl peroxide and chloroplatinic acid was studied.

2. It was shown that the activity of the double bond in monoallyl derivatives of silicon increases with the size of the alkyl radicals, and on replacement of the latter by electronegative phenyl radicals or chlorine atoms.

3. A series of hexaalkyl(phenyl) derivatives of disilylpropane were synthesized on the basis of the addition products of trichlorosilane with monoallyl derivatives of silicon; their structure was studied, and it was shown that the addition of trichlorosilane to trialkyl(phenyl, chloro) allylsilanes in the presence of benzoyl peroxide or chloroplatinic acid goes contrary to Markovnikov's rule.

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SYNTHESIS OF VINYL DERIVATIVES OF BIPHENYL, DIPHENYL OXIDE, AND DIPHENYL SULFIDE

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In order to study the effect of the nature of the substituent groups (phenyl, phenoxy, and phenylthio) on polymerization capacity and the properties of the polymers obtained, we synthesized o- and p-vinylbiphenyls, o- and p-vinyldiphenyl oxides, and p-vinyldiphenyl sulfide.

Vinyldiphenyl oxide was first prepared from diphenyl oxide through organomagnesium compounds [1]. There is a brief report on the synthesis of vinyldiphenyl sulfide in a patent [2], according to which it was obtained from diphenyl sulfide through the acetyl derivative. A more detailed study has been made of vinylbiphenyl, whose ortho and para isomers were prepared through organomagnesium derivatives [3-5] or by reaction of biphenyl with ethylene oxide by the Friedel-Crafts reaction [6, 7].

We prepared the carbinol of diphenyl oxide by the reaction of diphenyl oxide with ethylene oxide in the presence of aluminum chloride. We were unable to synthesize the carbinol of diphenyl sulfide by this method, but it was prepared through an organomagnesium compound.

EXPERIMENTAL

1. Synthesis of Vinylbiphenyl

a) Preparation of β-hydroxyethylbiphenyl. Aluminum chloride (86 g) was added in small portions with stirring to a solution of 100 g of biphenyl in chlorobenzene (450 ml) cooled to -10°. A 50% solution of ethylene oxide (63 g) was then added dropwise and the hydrogen chloride formed removed by suction with a water pump. After the addition, the mixture was stirred at room temperature for 1 hr and then poured into ice water acidified with hydrochloric acid. The hydrocarbon layer was separated, washed with water, and dried with anhydrous sodium sulfate. After the solvent had been removed, the unreacted biphenyl was separated from the reaction products by vacuum distillation. The fraction with b.p. 150-170° (2 mm) was the carbinol of biphenyl. The yield was 20%.

b) Preparation of vinylbiphenyl. Dehydration of the carbinol with potassium hydroxide by the usual method yielded a mixture of ortho and para isomers (60% and 40%, respectively) of vinylbiphenyl in a total yield of 47%. By cooling to -20° the p-vinylbiphenyl was separated from the ortho isomer, which was fractionally distilled. o-Vinylbiphenyl is a colorless liquid.

B.p. 112-113° (0.5 mm), $n^{18}D$ 1.6190. According to literature data [8]: b.p. 114-117° (1 mm), $n^{25}D$ 1.6168.

Found %: C 93.24; H 6.84. $C_{14}H_{12}$. Calculated %: C 93.33; H 6.67.

p-Vinylbiphenyl, recrystallized from alcohol, forms colorless crystals.

B.p. 124-126° (2 mm), m.p. 118-119°. According to literature data [8]: b.p. 136-138° (6 mm), m.p. 119°.

Found %: C 93.36; H 6.68. $C_{14}H_{12}$. Calculated %: C 93.33; H 6.67.

2. Synthesis of Vinyldiphenyl Oxide

a) Preparation of β-hydroxyethyldiphenyl oxide. The carbinol of diphenyl oxide was prepared from diphenyl oxide and ethylene oxide similarly to the synthesis of the carbinol of biphenyl. After two distillations, β-hydroxyethyldiphenyl oxide appeared as a viscous, colorless liquid with b.p. 145-148° (1 mm). The yield was 38%.

b) Preparation of vinyldiphenyl oxide. The carbinol was dehydrated with potassium hydroxide by the usual method. The total yield of the mixture of ortho and para isomers of vinyldiphenyl oxide was 70%. Fractional recrystallization at -20° yielded o-vinyldiphenyl oxide with m.p. 38-39° and p-vinyldiphenyl oxide with b.p. 106° (1 mm), $n^{20}D$ 1.6014.

According to literature data [8]: o-vinyldiphenyl oxide melts at 39° and p-vinyldiphenyl oxide has $n^{25}D$ 1.6006 and d^{20}_4 1.062.

Found %: C 85.63; H 6.49. $C_{14}H_{12}O$. Calculated %: C 85.68; H 6.16.

3. Synthesis of p-Vinyldiphenyl Sulfide

a) Preparation of β-hydroxyethyldiphenyl sulfide. A solution of 75 g of ethylene oxide in 75 ml of absolute ether was added to the Grignard reagent prepared from 224 g of bromodiphenyl sulfide, 21 g of magnesium turnings, and 300 ml of absolute ether. Toward the end of the addition of the ethylene oxide solution the reaction mixture thickened. At the end of the reaction the ether was removed by distillation. The reaction mass was decomposed with a mixture of ice and sulfuric acid. The carbinol of diphenyl sulfide was extracted with benzene, washed with water, and dried with anhydrous magnesium sulfate. After removal of the benzene, the residue was vacuum distilled. After recrystallization from 80% alcohol, the carbinol had m.p. 55-56°. The yield was 18%.

b) Preparation of p-vinyldiphenyl sulfide. The β-hydroxyethyldiphenyl sulfide was dehydrated with potassium hydroxide by the usual method. The yield of p-vinyldiphenyl sulfide was 56%. After vacuum distillation, the compound appeared as a colorless liquid.

B.p. 137° (1 mm), $n^{20}D$ 1.6495, d^{20}_4 1.096. According to literature data [3]: b.p. 135-140° (1 mm).

Found %: C 79.45; H 5.76. $C_{14}H_{12}S$. Calculated %: C 79.28; H 5.66.

SUMMARY

1. The most convenient method of preparing vinyl derivatives of biphenyl and diphenyl oxide is the addition of ethylene oxide to biphenyl and diphenyl oxide (in the presence of anhydrous aluminum chloride as catalyst), with subsequent dehydration of the carbinols formed. It was shown that this yields the ortho and para isomers of vinylbiphenyl and vinyldiphenyl oxide.

2. The method of preparing p-vinyldiphenyl sulfide was improved.

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OXIDATION OF 1-ALKYL-1-CYCLOPENTENES BY PERFORMIC ACID AS A METHOD OF SYNTHESIZING 2-ALKYL-1-CYCLOPENTANONES

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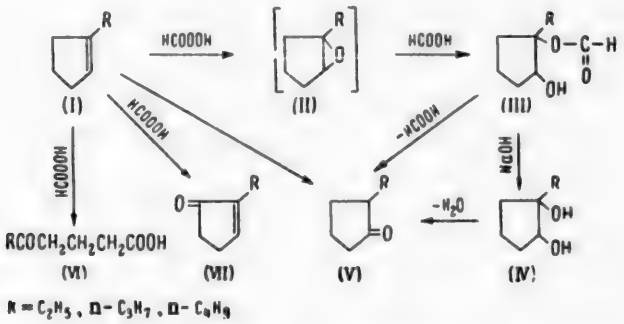
Performic acid oxidation of 1-methyl-1-cyclopentene with subsequent dehydration of the secondary-tertiary glycol yielded 2-methyl-1-cyclopentanone [1]. We decided to use this method to prepare 2-ethyl -1-cyclopentanone, 2-n-propyl-1-cyclopentanone, and 2-n-butyl-1-cyclopentanone, which we required for the synthesis of 1,2-dialkylcyclopentanes [2].

As a result of studying the oxidation of 1-alkyl-1-cyclopentenes with performic acid, we showed that ketones (V) could be obtained both with isolation of the intermediate products (III) and (IV) and without their isolation, in one stage.



If the water and formic acid are distilled from the oxidation products of 1-alkyl-1-cyclopentenes [3] at atmospheric pressure, as a result of the reaction of the glycol monoformates formed with formic acid, 1-alkyl-1-cyclopentanones are formed in one stage. The constants of the ketones obtained are given in Table 1.

Distillation of the formic acid and water from the oxidation products under reduced pressure (about 40-45 mm) yielded monoformates of trans-1-ethyl-1,2-cyclopentanediol, trans-1-n-propyl-1,2-cyclopentanediol, and trans-1-n-butyl-1,2-cyclopentanediol. The structure of these monoformates follows from their formation scheme in accordance with data on the direction of opening of an α-oxide ring under the action of acids [4, 5].

Hydrolysis of the glycol monoformates with alkali yielded trans-1-ethyl-1,2-cyclopentanediol, trans-1-n-propyl-1,2-cyclopentanediol, and trans-1-n-butyl-1,2-cyclopentanediol. The trans configuration assigned to the glycols follows from the preparation scheme of the latter through the intermediate formation of α-oxides and their subsequent cleavage under the action of acids [6]. The constants of the glycols and their monoformates are given in Table 2.

TABLE 1

Constants of 2-Alkyl-1-cyclopentanones and 1-Alkylcyclopent-2-en-1-ones Obtained

Number	Ketones	Hydrocarbon oxidized (in moles)	Ketone yield (in %)	Boiling point (pressure in mm)	Crystallization point*	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found, (%) C	Found, (%) H	Calculated (%) C	Calculated (%) H
1	2-Ethyl-1-cyclopentanone	10.18	65.7	160.5° (745), 53–54 (12)	—73.4	1.4399	0.9117	32.42	32.34	—	—	—	—
2	2-n-Propyl-1-cyclopentanone	2.84	66.3–70.4	181.5 (743)	—68.4	1.4426	0.9016	37.08	36.96	—	—	—	—
3	2-n-Butyl-1-cyclopentanone	3.63	66.5	70.5 (6), 54.5 (2)	—39	1.4462	0.8957	41.76	41.57	76.92, 76.99	11.51, 11.67	77.09	11.50
4	2-Ethylcyclopent-2-en-1-one	—	—	176.0 (745)	—	1.4830	0.9700	32.43	31.87	75.40, 75.60	8.98, 9.16	76.32	9.15
5	2-n-Propylcyclopent-2-en-1-one	—	—	191.6 (473)	—	1.4780	0.9484	37.06	36.49	76.82, 77.00	9.89, 9.90	77.37	9.74

Note: Literature data for substances: No. 1, b.p. 159-160° (751), m.p. -72.5°, $n^{20}D$ 1.4398, d^{20}_4 0.9119 [14]; No. 2, b.p. 183.1-183.2° (760), m.p. - 68.25°, $n^{20}D$ 1.4429, d^{20}_4 0.9017 [15]; No. 3, b.p. 89° (10) [16], 196-198°, $n^{30}D$ 1.4418 [17]; Nos. 4 and 5 have not been described in the literature.

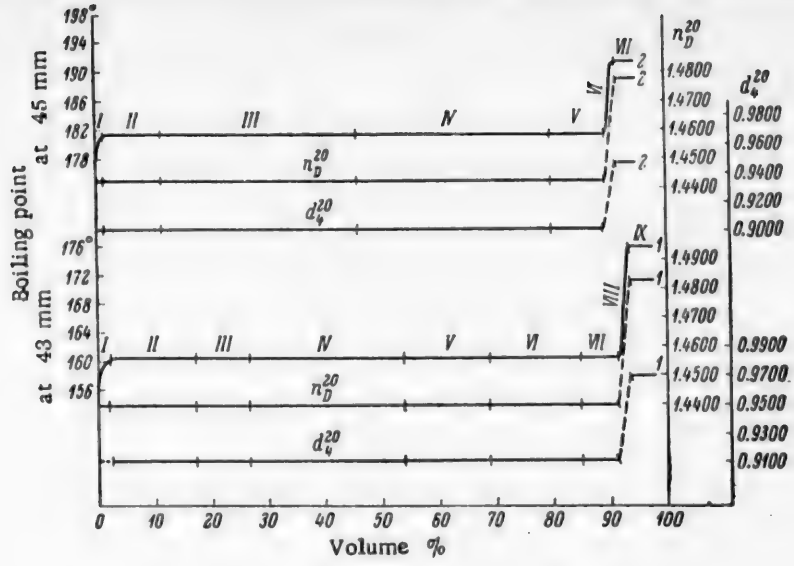
*The crystallization point was determined in the Chemical Thermodynamic Laboratory of Moscow State University by A. G. Anikin and G. M. Dugacheva, whom we take this opportunity to thank.

TABLE 2

Constants of trans-1-Alkyl-1, 2-cyclopentanediols Obtained and Their Monoformates*

Name	Amt. of starting materials (in moles)	Yield of glycols, their monoformates, %	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found (%) C	Found (%) H	Calculated (%) found	Calculated (%) calculated
trans-1-Ethyl-1,2-cyclopentanediol	0.26	91.8	98° (5) M.p. 73–74°.	—	—	—	—	64.86, 64.80	10.90, 10.80	64.58	10.84
Its monoformate	1.0	45.8	83–84 (3)	1.4681	1.0770	40.84	40.12	60.61, 60.70	9.29, 9.40	60.74	8.92
trans-1-n-propyl-1,2-cyclopentanediol	0.07	98.0	105–106 (4)	1.4842	1.0389	39.73	39.99	66.66, 66.63	11.15, 11.18	66.62	11.18
Its monoformate	0.5	52.8	237–238 (748), 86 (2)	1.4628	1.0550	44.94	44.74	62.29, 62.40	9.24, 9.22	62.76	9.37
trans-1-n-Butyl-1,2-cyclopentanediol	1.0	98.6	120–121 (5)	1.4830	1.0131	44.61	44.61	68.53, 68.51	11.14, 11.20	68.31	11.47
Its monoformate	3.75	63.9	94 (3)	1.4645	1.0317	49.85	49.36	64.40, 64.52	9.78, 9.92	64.49	9.74

*None of the compounds obtained have been described in the literature; they all vitrified on cooling.



Distillation curves of ketones obtained by oxidation of 1-ethyl-1-cyclopentene (1) and 1-n-propyl-1-cyclopentene (2) and constants of fractions.

For the preparation of 2-n-butyl-1-cyclopentanone with the isolation of the intermediate products, trans-1-n-butyl-1,2-cyclopentanediol was dehydrogenated in the presence of iodine.

The action of acids on the monoformates of the glycols yielded the same ketones as mentioned above. The best yields were obtained by boiling the glycol monoformates with dilute sulfuric or 85% formic acid.

From the oxidation products of 1-ethyl-1-cyclopentene, 1-n-propyl-1-cyclopentene, and 1-n-butyl-1-cyclopentene we also isolated 5-ketoheptanoic, 5-ketooctanoic, and 5-ketononanoic acids (VI) and as the size of the radical on the carbon atom at the double bond increased, the yield of keto acid increased from 2.5 to 14.2%. As the cleavage of a C = C bond by reagents of a peroxide nature is possible when the carbon atoms are already partially oxidized [7], the formation of keto acids apparently occurs as a result of further oxidation by performic acid of glycol monoformates, which are the main oxidation products. The constants of the keto acids obtained are given in Table 3.

When the ketones obtained by oxidation of 1-ethyl-1-cyclopentene and 1-n-propyl-1-cyclopentene were distilled on a column, it was observed that together with the saturated cyclic ketones 2-ethyl-1-cyclopentanone and 2-n-propyl-1-cyclopentanone, the oxidation products also contained unsaturated ketones, whose constants were somewhat higher than those of the corresponding saturated ketones (see Table 1 and figure). The ratio of the amounts of the saturated 2-ethyl-1-cyclopentanone and 2-n-propyl-1-cyclopentanone to the amounts of the corresponding unsaturated ketones was 18 : 1, and 23.5 : 1.

Hydrogenation of these ketones yielded 2-ethyl-1-cyclopentanone and 2-n-propyl-1-cyclopentanone, respectively, which demonstrated the position of the carbonyl group; to determine the position of the double bond we plotted ultraviolet absorption spectra of the ketones themselves and also their derivatives and these data are given in Table 4. Literature data on the absorption of related compounds [8, 9] are given for comparison. The data in Table 4 show that the absorption spectra of the ketones investigated, which are in good agreement with literature data, demonstrate that the unsaturated ketones contained a double bond conjugated with the carbonyl group, since unsaturated ketones (and their derivatives) containing an unconjugated double bond are known to have spectral characteristics that are identical with saturated ketones.

Consequently, on the basis of the ultraviolet absorption spectra and the results of hydrogenation, the structures of 2-ethylcyclopent-2-en-1-one and 2-n-propylcyclopent-2-en-1-one must be assigned to the unsaturated ketones. •

•We would like to thank L. A. Kazitsyna for help in discussing the spectral data and establishing the structure of the unsaturated ketones.

TABLE 3

Constants of Keto Acids Obtained

No.	Keto acids	Hydrocarbon oxidized (in moles)	Keto acid yield (in %)	Boiling point (pressure, mm)	Melting point
1	5-Ketoheptanoic	11.18	2.5	136–137°(4)	48.5°
2	5-Ketooctanoic	3.34	9.5	135.5–136 (2)	33–34
3	5-Ketononanoic	3.63	14.2	140–141 (2)	43

Note: Literature data on keto acids: No. 1, b.p. 152-153° (9) [18], m.p. 50° [19]; No. 2, b.p. 147-148° (7) [20], m.p. 34° [19]; No. 3, b.p. 142° (2), m.p. 40° [19], 43.5° [18].

TABLE 4

Ultraviolet Absorption Spectra of Ketones and Their Derivatives

Ketones	λ_{max} (in mμ)	lg ε	Ketone semicarbazones		Ketone 2,4-dinitrophenylhydrazones	
			λ_{max} (in mμ)	lg ε	λ_{max} (in mμ)	lg ε
2-Ethyl-1-cyclopentanone	300	1.35	230	4.20	346	4.05
2-n-Propyl-1-cyclopentanone	298	1.32	230	4.00	346	3.61
Cyclopentanone	299	1.30 [8]	—	—	—	—
Cyclohexanone	285	1.15 [8]	229.5	4.05 [8]	345	4.26 [9]
2-Methyl-1-cyclopentanone	—	—	—	—	344	4.20 [9]
2-Ethylcyclopent-2-en-1-one	326 *	1.79	261	4.39	363	3.96
2-n-Propylcyclopent-2-en-1-one	328 *	1.54	263	4.20	363	3.77
1-Methylcyclohex-1-en-3-one	310	1.68 [8]	265.5	4.41 [8]	—	—
2-Methylcyclohex-2-en-1-one	—	—	—	—	362	4.34 [9]
Mesityl oxide	313.5	1.78 [8]	260	4.08 [8]	364	4.26 [9]
2-Methylcyclopent-2-en-1-one	—	—	—	—	365 [9]	—
2-Methylcyclopent-4-en-1-one	—	—	—	—	371 [9]	—

* The somewhat high displacement of the absorption band for 2-alkylcyclopent-2-en-1-ones may be explained by higher strain in the five-membered ring. Probably this may also explain the appearance of a weakly expressed vibrational structure in the spectra of cyclopentanones and cyclopentenones.

This oxidation of a methylene group in a position α to a double bond is also observed in the oxidation of unsaturated compounds by atmospheric oxygen [10], selenium dioxide [11], or hydrogen peroxide in the presence of vanadium pentoxide [12].

The formation of unsaturated ketones under the action of organic peracids, like the cleavage of a double bond with the formation of keto acids, has not been described in the literature and we were the first to observe it.

The single-stage synthesis of 2-alkyl-1-cyclopentanones by oxidation of 1-alkyl-1-cyclopentenes with performic acid which we developed presents no experimental difficulties, requires a short time, and has a number of advantages as regards ketone yields in comparison with other methods of preparing them.

TABLE 5

Constants of the Semicarbazones and 2,4-Dinitrophenylhydrazones of the 2-Alkyl-1-cyclopentanones, 2-Alkylcyclopent-2-en-1-ones, and Keto Acids Obtained

Sample No.	Name	Melting point•	Found (%)••••			Calculated (%)		
			C	H	N	C	H	N
1	Semicarbazone of 2-ethyl-1-cyclopentanone(from alcohol)	188—189° (decomp) [14]	56.40, 56.60	8.99, 8.84	24.81, 25.04	56.78	8.94	24.83
2	2,4-Dinitrophenylhydrazone(from alcohol)	158—159 ••	53.45, 53.17	5.58, 5.52	18.57, 18.55	53.42	5.52	19.17
3	Semicarbazone of 2-ethylcyclopent-2-en-1-one (from acetone)	191.7—192.7 (decomp) ••	57.40, 57.30	7.94, 7.81	25.39, 25.72	57.47	7.83	25.14
4	2,4-Dinitrophenylhydrazone [from a mixture of alcohol and ethyl acetate (1 : 1)]	192—193 ••	54.03, 54.04	4.97, 4.87	19.17, 18.99	53.79	4.86	19.30
5	Semicarbazone of 2-n-propyl-1-cyclopentanone (from alcohol)	206—207 (decomp)[22,15]	58.65, 58.84	9.29, 9.30	22.80, 23.07	58.98	9.35	22.93
6	2,4-Dinitrophenylhydrazone (from alcohol)	154.5—155.5 [23]	54.88, 55.14	6.00, 6.04	17.81, 17.71	54.89	5.92	18.29
7	Semicarbazone of 2-n-propylcyclopent-2-en-1-one (from benzene)	184—185 (decomp) ••	59.51, 59.75	8.25, 8.35	23.38, 23.08	59.64	8.34	23.19
8	2,4-Dinitrophenylhydrazone (from a mixture of alcohol and ethyl acetate)	211—212 (decomp)•••	55.54, 55.35	5.31, 5.34	19.05, 18.93	55.25	5.30	18.41
9	Semicarbazone of 2-n-butyl-1-cyclopentanone (from alcohol)	193.5—194 [17]	60.77, 60.86	9.67, 9.61	21.46, 21.36	60.88	9.71	21.30
10	2,4-Dinitrophenylhydrazone (from alcohol)	115—116 ••	56.50, 56.54	6.38, 6.44	18.21, 18.05	56.24	6.29	17.49
11	Semicarbazone of 5-ketoheptanoic acid (from anhydrous alcohol)	190—191 [18]	47.90, 47.96	7.66, 7.54	20.71, 20.94	47.74	7.51	20.88
12	Semicarbazone of 5-ketooctanic acid (from alcohol)	194—195 (decomp)[20]	50.19, 50.32	7.90, 7.90	19.60, 19.55	50.22	7.96	19.52
13	Semicarbazone of 5-ketononanoic acid (from alcohol)	140—141 [18]	52.18, 52.10	8.32, 8.22	18.30, 18.19	52.38	8.35	18.33

• The melting points of all the compounds were determined in a copper block previously heated to a temperature 15-20° below the melting point of the compound. The heating rate during the melting point determination was 4°/min.

•• Not described in the literature.

••• The m.p. 92-92.5° is given in the literature, but the ketone itself was not isolated and its structure was not demonstrated strictly [24].

•••• The analyses were carried out in the Analytical Laboratory of the Institute of Organic Chemistry, Academy of Sciences, USSR.

EXPERIMENTAL

Oxidation of unsaturated hydrocarbons with performic acid. Three hydrocarbons were oxidized: 1-ethyl-1-cyclopentene, 1-n-propyl-1-cyclopentene, and 1-n-butyl-1-cyclopentene [3]. Into a three-necked, 2-liter flask with a mechanical stirrer, thermometer, and dropping funnel were placed 600 ml (13.2 moles) of 85% formic acid and 150 ml (1.5 moles) of 30% hydrogen peroxide. The mixture was heated to 40° on a water bath for 5 min and then 1 mole of unsaturated hydrocarbon was gradually added at such a rate that the temperature of the reaction mixture remained at the level of 40-45°, with the flask with the reaction mixture cooled in ice water. When all the hydrocarbon had been added (this required 20-25 min), the mixture was stirred for another hour at the same temperature with the flask cooled at times. During this time the temperature of the reaction mixture began to fall, indicating the end of the reaction. The reaction mixture was left overnight and on the following day the unreacted hydrogen peroxide content was determined [13]. If hydrogen peroxide was present it was destroyed by shaking the solution with ferrous sulfate. The reaction products were then treated to prepare ketone or monoformate.

Preparation of ketones. The formic acid and water were distilled from the reaction mixture at atmospheric pressure; as soon as the liquid boiled, the reaction mixture darkened strongly. Together with the formic acid and water, the ketone formed distilled and the boiling point of this mixture was 106-110°. The ketone in the distillate separated as an oily layer. The distillate was neutralized in the cold with small portions of concentrated alkali solution to a weakly alkaline reaction to litmus. The ketone liberated was dissolved in ether, the aqueous layer extracted several times with small portions of ether, and the ether extracts added to the ether solution of the ketone. The residue in the distillation flask was diluted with 100 ml of ether, transferred to a separating funnel, and treated several times with small portions of cooled 10% alkali solution to remove the keto acid formed during the oxidation and also the residual formic acid, and then with water. The ether solutions of the ketone were combined and dried with baked potassium carbonate. After removal of the ether, the ketone was vacuum distilled.

By distillation at atmospheric pressure on a column with a metallic packing and an efficiency of 80 theoretical plates, from 293 g of 2-ethyl-1-cyclopentanone obtained by this method we obtained 265 g of 2-ethyl-1-cyclopentanone (93.1% of the total amount of ketones) and 14.7 g of 2-ethylcyclopent-2-en-1-one (5.2% of the total amount of ketones). The distillation curve of the ketones is given in the figure.

Hydrogenation of 1.8 g of 2-ethylcyclopent-2-en-1-one at room temperature over Raney nickel in alcohol solution gave 2-ethyl -1-cyclopentanone; the semicarbazone had m.p. 188-189° (decomp., from alcohol); the 2,4-dinitrophenylhydrazone had m.p. 158-159° (from alcohol). Mixed samples with the semicarbazone and 2,4-dinitrophenylhydrazone of authentic 2-ethyl-1-cyclopentanone did not show depression of melting point.

Another portion (457 g) of 2-ethyl-1-cyclopentanone was purified through the semicarbazone. The recrystallized semicarbazone yielded 287 g of 2-ethyl-1-cyclopentanone (62.8% of the weight of the unpurified ketone). Thus distillation on a column was the most efficient method of purifying the ketone.

Distillation on a column of 238 g of the ketone isolated from the oxidation products of 1-n-propyl-1-cyclopentene yielded 210 g of 2-n-propyl-1-cyclopentanone (93.9% of the total amount of ketones) and 9 g of 2-n-propylcyclopent-2-en-1-one (4.0% of the total amount of ketones). The distillation curve of the ketones is given in the figure (see p. 951).

As described above, 1.5 g of 2-n-propylcyclopent-2-en-1-one was hydrogenated to 2-n-propyl-1-cyclopentanone; the semicarbazone had m.p. 206-207° (decomp., from alcohol); the 2,4-dinitrophenylhydrazone had m.p. 154.5-155.5° (from alcohol). Mixed samples with the semicarbazone and 2,4-dinitrophenylhydrazone of authentic 2-n-propyl-1-cyclopentanone did not show depression of melting point.

2-n-Butyl-1-cyclopentanone (602 g) was purified through the semicarbazone; the recrystallized semicarbazone yielded 465 g of pure ketone. Decomposition of the semicarbazone isolated from the mother liquor yielded 26 g of ketone with somewhat high constants ($n^{20}D$ 1.4490, d^{20}_4 0.8994), apparently as a result of the presence of some unsaturated ketone (2-n-butylcyclopent-2-en-1-one) which could have been formed during the oxidation (see above).

The constants and yields of the ketones are given in Table 1 and the constants of the semicarbazones and 2,4-dinitrophenylhydrazones are in Table 5. The ultraviolet absorption spectra of the unsaturated ketones are given in Table 4.

Preparation of monoformates. The formic acid and water were removed from the reaction mixture in vacuum (40-45 mm); a small amount of ketone formed also distilled. The distillate containing the ketone and the residue in the distillation flask, which was mainly the monoformate of trans-1-alkyl-1,2-cyclopentanediol, were treated as above in the preparation of the ketone. The glycol monoformates were thick liquids which did not crystallize on cooling; their constants are given in Table 2. In addition to monoformates and a small amount of keto acids, the oxidation products of 1-alkyl-1-cyclopentenes yielded 13.2% of 2-ethyl-1-cyclopentanone, 7% of 2-n-propyl-1-cyclopentanone, and 14.3% of 2-n-butyl-1-cyclopentanone, respectively.

The monoformate of trans-1-n-propyl-1,2-cyclopentanediol was also distilled at atmospheric pressure without decomposition.

Reaction of monoformates with acids. Treatment of 16.2 g of the monoformate of trans-1-ethyl-1,2-cyclopentanediol with 50 ml of concentrated hydrochloric acid at room temperature yielded 6.7 g (58.7%) of 2-ethyl-1-cyclopentanone.

Treatment of 16.5 g of the monoformate of trans-1-n-propyl-1,2-cyclopentanediol with 50 ml of 85% formic acid yielded 9.0 g (75%) of 2-n-propyl-1-cyclopentanone.

From 180 g of the monoformate of trans-1-n-butyl-1,2-cyclopentanediol and 100 ml of 5% sulfuric acid we obtained 106 g (78.1%) of 2-n-butyl-1-cyclopentanone. Treatment of 20 g of the monoformate with a few drops of concentrated sulfuric acid yielded only 4.6 g (30.6%) of ketone.

trans-1-Alkyl-1,2-cyclopentanediols were obtained by hydrolysis of the corresponding monoformates with concentrated alkali in the usual way. trans-1-Ethyl-1,2-cyclopentanediol was a crystalline product and the other two glycols were thick, almost immobile liquids which did not crystallize on cooling. Their constants are given in Table 2.

Attempt to oxidize trans-1-ethyl-1,2-cyclopentanediol. trans-1-Ethyl-1,2-cyclopentanediol (20 g) was oxidized with performic acid as described above, with the exception that when all the glycol had been added, the mixture was stirred at 40-45° for 3 hr and then heated for 2 hr at 70-75°. As a result of dehydration of the unoxidized glycol, distillation of the formic acid and water at atmospheric pressure yielded 2-ethyl-1-cyclopentanone (b.p. 56-57° at 17 mm, $n^{20}D$ 1.4403); the yield was 14.9 g (86.6%); and we also obtained 0.9 g of 5-ketoheptanoic acid.

Dehydration of trans-1-n-butyl-1,2-cyclopentanediol. 1-n-Butyl-1,2-cyclopentanediol (140 g) was dehydrated with a few crystals of iodine; we obtained 99.5 g (80.2% and 83.6% in one experiment) of 2-n-butyl-1-cyclopentanone.

The keto acids were isolated in the usual way from alkaline extracts obtained by treating the oxidation products of 1-alkyl-1-cyclopentenes with 10% alkali solution.

The constants of the keto acids are given in Table 3 and those of their semicarbazones in Table 5.

SUMMARY

1. The oxidation of 1-ethyl-1-cyclopentene, 1-n-propyl-1-cyclopentene, and 1-n-butyl-1-cyclopentene with performic acid was studied. The main oxidation products are the monoformates of the corresponding glycols; at the same time, as a result of oxidation of a methylene group in a position α to the double bond, unsaturated cyclic ketones are formed and there is also cleavage of the double bond with the formation of keto acids.

2. trans-1-Ethyl-1-2,cyclopentanediol, trans-1-n-propyl-1,2-cyclopentanediol, and trans-1-n-butyl-1,2-cyclopentanediol and their monoformates were prepared for the first time.

3. A method is proposed for the synthesis of 2-alkyl-1-cyclopentanones in one stage by the oxidation of 1-alkyl-1-cyclopentenes; this method gives 2-ethyl-1-cyclopentanone, 2-n-propyl-1-cyclopentanone, and 2-n-butyl-1-cyclopentanone in yields of 65-67%.

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SYNTHESIS OF α,γ-DINITRO KETONES

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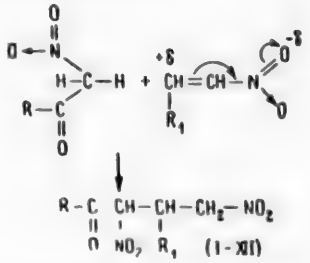
Nitro ketones are used successfully as starting materials for the synthesis of various pharmacologically active substances, namely, analogs of quinacridine, adrenalin, chloromycetin, and myosmin.

Our attention was attracted to α-nitro ketones, in which one would expect the hydrogen atoms of the methylene groups to be markedly labile due to π,σ-conjugation with the electrophilic nitro and carbonyl groups.

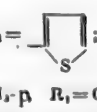
Up to now there have been no attempts to react α-nitro ketones with compounds with active double bonds, in particular, unsaturated nitro compounds, which react readily with substances which contain labile hydrogen atoms in methylene and methyl groups [1-4].

In order to develop a general method of synthesizing α,γ-dinitro ketones and subsequently heterocyclizing their reduction products, we reacted certain aliphatic-aromatic α-nitro ketones, namely, ω-nitroacetophenone and p-methyl-p-methoxy- and m,p-methylenedioxy-ω-nitroacetophenones, with unsaturated nitro compounds of the aromatic and heterocyclic series: β-nitrostyrene, p-methoxy- and p-nitro-β-nitrostyrenes, 1,4-bis(β-nitrovinyl)benzene, and 2-furyl- and 2-thienylnitroethylenes.



(I) $R=C_6H_5$, $R_1=C_6H_5$; (II) $R=C_6H_5$, $R_1=C_6H_4NO_2$-p;

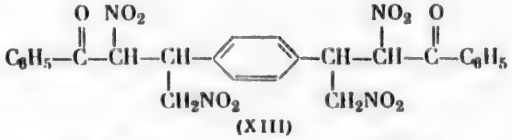
(III) $R=C_6H_5$, $R_1=C_6H_4OCH_3$-p; (IV) $R=C_6H_5$, $R_1=$;

(V) $R=C_6H_5$, $R_1=$  ; (VI) $R=C_6H_4OCH_3$-p, $R_1=C_6H_5$;

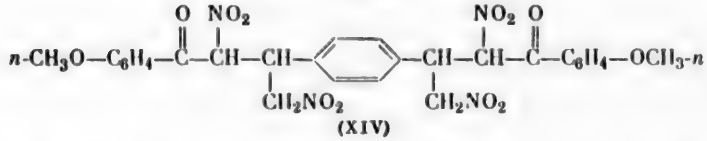
(VII) $R=C_6H_4OCH_3$-p, $R_1=C_6H_4NO_2$-p; (VIII) $R=C_6H_4OCH_3$-p, $R_1=C_6H_4OCH_3$-p;
(IX) $R=C_6H_4CH_3$-p, $R_1=C_6H_5$; (X) $R=C_6H_4CH_3$-p, $R_1=C_6H_4NO_2$-p;
(XI) $R=C_6H_3CH_2O_2$-m,p, $R_1=C_6H_5$;
(XII) $R=C_6H_3CH_2O_2$-m,p, $R_1=C_6H_4NO_2$-p.

1,4-bis(β-Nitrovinyl)benzene reacted with two moles of ω-nitroacetophenone and p-methoxy-ω-nitroacetophenone; both compounds added at both double bonds of the dinitroolefin.

Substance	Melting point	Found (%)			Calculated (%)			Yield (in %)
		C	H	N	C	H	N	
(I)	106—112° (n-hexane + benzene)	60.90, 61.36	4.68	9.02	61.14	4.49	8.91	85
(II)	155—156 (80% acetic acid)	53.69, 53.54	4.22, 4.04	11.90, 11.90	53.48	3.65	11.7	85
(III)	106—109 (n-hexane + benzene)	59.04	4.93	8.12	59.30	4.68	8.14	85
(IV)	71—75 (n-hexane + benzene)	55.00, 55.48	3.93, 4.12	9.32, 9.45	55.26	3.98	9.21	54
(V)	113—115 (ethanol)	52.54, 52.49	4.36, 4.71	8.78, 8.91	52.16	4.38	8.70	62
(VI)	106—112	59.05, 59.12	4.76, 4.85	8.05, 8.14	59.30	4.68	8.14	78
(VII)	148—148.5 (benzene + ligroin)	52.67, 52.38	3.56, 3.79	11.12, 10.68	52.44	3.88	10.79	90
(VIII)	125.5—128.5 (n-hexane + benzene)	57.92, 57.88	4.92, 4.79	7.65, 7.73	57.75	4.85	7.48	80
(IX)	94—96 (n-hexane + benzene)	—	—	8.40, 8.47	—	—	8.53	50
(X)	143—144 (ethanol)	54.76, 54.94	3.86, 4.16	11.37, 11.29	54.69	4.05	11.26	81.5
(XI)	114—117 (ethanol)	56.84, 56.84	3.84, 4.14	8.02, 7.89	56.98	3.94	7.80	67.5
(XII)	155—155.5 (n-hexane + benzene)	50.87, 50.86	2.99, 3.39	10.49, 10.40	50.63	3.25	10.42	87.5
XIII)	184—185 (acetone + ethanol)	56.56, 56.40	4.82, 4.52	10.14, 10.18	56.73	4.03	10.18	85
(XIV)	187—187.5	55.11, 54.90	4.29, 4.36	9.01, 8.89	55.08	4.29	8.96	57



(XIII)



(XIV)

On the basis of the capacity of α-nitro ketones for keto-enol and nitro-aci-nitro tautomerism [5-7], one might have expected the formation of both C and O derivatives. However, the structure of the products from their reaction with nitroolefins confirmed the hypothesis on the reaction of the ketonic forms of α-nitro ketones through the methylene group.

The failure of attempts to induce the nitro ketones investigated to react with aliphatic nitroolefins (nitroethylene, nitropentene, nitroisopentene, and nitroisohexene) may be explained by the ready polymerizability of the latter. It is assumed that under the given conditions, the polymerization rate of the nitroolefins exceeds the rate of their reaction with nitro ketones due to the high activity of the double bond.

EXPERIMENTAL

The reaction of nitro ketones with unsaturated nitro compounds was carried out in boiling benzene or methanol (product V) with triethylamine as catalyst and was complete in 5-10 min; the synthesis of substances (VIII) and (IX) only proceeded in acetone at room temperature over a period of 5 days.

The reaction of 2-furyl- and 2-thienylnitroethylene with nitroacetophenone was accompanied by considerable tar formation by (IV) and (V).

The melting points of the products, their analysis results, and the yields are given in the table.

SUMMARY

α, γ-Dinitro ketones were synthesized by condensation of α-nitro ketones with nitroolefins.

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HYDROLYSIS OF N-CHLORO- AND N-TRICHLOROACETYLARENESULFONAMIDES

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Arenesulfonamides and their N-alkyl derivatives are hydrolyzed by boiling with dilute mineral acids, with rupture of the bond between the sulfur and nitrogen atoms at considerably lower rates than carbonamides [1].

It has been shown [2] that N-formylarenesulfonamides are hydrolyzed rapidly in acid solution with the liberation of HCN, i.e., the bond between the sulfur and nitrogen atoms is ruptured. It seemed to us that N-chloro- and N-trichloroacetylarenesulfonamides [3], which are simultaneously amides of arenesulfonic and chloro- or trichloroacetic acids, should be hydrolyzed readily with rupture of the bond between the carbon and nitrogen atoms and the formation of arenesulfonamides. We carried out appropriate experiments to determine the actual direction of the hydrolysis of N-chloro- and N-trichloroacetylarenesulfonamides.

It was established that N-chloro- and N-trichloroacetylarenesulfonamides are hydrolyzed when boiled in water, 5% sulfuric acid, and alkaline media, with rupture of the bond between the nitrogen and carbon atoms and the formation of arenesulfonamides according to the scheme:

$$ArSO_2NHCOCH_2Cl + HOH \longrightarrow ArSO_2NH_2 + CH_2ClCOOH$$
$$ArSO_2NHCOCCl_3 + HOH \longrightarrow ArSO_2NH_2 + CCl_3COOH.$$

The presence of arenesulfonamides among the hydrolysis products was demonstrated by determining the melting points of the pure materials, and mixed melting points, and from the chemical properties. The yield of arenesulfonamides was determined by titration of the unhydrolyzed N-chloro- and N-trichloroacetylarenesulfonamides with alcoholic alkali in an alcohol medium.

The formation of chloroacetic acid during the hydrolysis of N-chloroacetylarenesulfonamides was established by separating it from the arenesulfonamide by steam distillation after the hydrolysis and determining the equivalent by titration of the distillate with alkali. Under the hydrolysis conditions, i.e., in a boiling mixture, the trichloroacetic acid formed during the hydrolysis of trichloroacetylarenesulfonamides was cleaved with the formation of chloroform and carbon dioxide: $CCl_3COOH \rightarrow CHCl_3 + CO_2$.

The presence of chloroform was demonstrated by isolating it in a pure form and by qualitative reactions [4].

N-Trichloroacetylarenesulfonamides are hydrolyzed more readily than N-chloroacetylarenesulfonamides. The data presented below in the table show that the hydrolysis of N-trichloroacetylbenzenesulfonamide was complete after 30 min while the complete hydrolysis of N-chloroacetylarenesulfonamide required 2 hr. The reason for this is apparently the higher polarization of the bond between the carbon and nitrogen atoms, caused by the effect of the trichloroacetyl group.

From the data in the same table it follows that the hydrolysis of N-chloro- and N-trichloroacetylarenesulfonamides in 5% solutions of sulfuric acid and alkali and in water occurs in approximately the same time. The sodium salts of N-chloroacetylarenesulfonamides are also hydrolyzed when their aqueous solutions are boiled.

Sample No.	Starting material	Medium	Hydrolysis time (in hr)	Arenesulfonamide yield (in %)
1	$C_6H_5SO_2NHCOCH_2Cl$	Water	0.5	51.9
2			1	82.9
3			1.5	93.1
4			2	100
5		5% H_2SO_4	3	100
6		5% NaOH	3	100
7	$C_6H_5SO_2NNaCOCH_2Cl$	Water	5	100
8	$p\text{-}CH_3C_6H_4SO_2NHCOCH_2Cl$	Water	0.5	3.3
9			1	36.8
10			1.5	67.5
11			2	83.1
12			4	100
13	$2,4,6\text{-}(CH_3)_3C_6H_2SO_2NHCOCH_2Cl$	Water	2	1.7
14	$C_6H_5SO_2NHCOCCl_3$	"	0.5	100
15		5% H_2SO_4	0.5	100
16		5% NaOH	0.5	100
17	$p\text{-}CH_3C_6H_4SO_2NHCOCCl_3$	Water	2	98
18	$2,4,6\text{-}(CH_3)_3C_6H_2SO_2NHCOCCl_3$		7.5	100
19	$p\text{-}(CH_3)_2CHC_6H_4SO_2NCOCCl_3$		10	100

The experimental results also show that N-chloro- and N-trichloroacetylarenesulfonamides are more resistant to hydrolysis after alkyl radicals have been introduced into the benzene nucleus and we were the first to observe this. The reason for this effect of alkyl radicals is apparently a decrease in the solubility of the corresponding arenesulfonamides and hence a slowing of the hydrolysis.

The relative resistance of N-chloro- and N-trichloroacetylarenesulfonamides to hydrolysis makes it possible to replace extraction with ligroin for separation from unreacted arenesulfonamide by neutralization with aqueous alkali in their preparation [3]. Filtration removes the arenesulfonamide, which is insoluble in a neutral medium, and acidification of the filtrate liberates N-chloro- and N-trichloroacetylarenesulfonamides.

EXPERIMENTAL

Into a flask with a reflux condenser were introduced 1 g of N-chloro- or N-trichloroacetylarenesulfonamide and either 20 ml of water, 19 ml of water and 1 g of H_2SO_4, or 19 ml of water and 1 g of NaOH. The flask contents were boiled until hydrolysis was complete. The hydrolysis was considered complete when the last sample of a series taken from the flask every 30 min did not give an acid reaction or a reaction for chlorine after a wash with water. Experiments 4-7, 12, and 14-19 were carried out in this way.

In addition, a series of experiments were carried out with partial hydrolysis over a definite time for determining the degree of hydrolysis after a given time (Expts. No. 1-3, 8-11, and 13).

In all experiments, after the hydrolysis, the flask contents were cooled and the precipitate collected by filtration, washed with water, dried, and its content of unreacted N-chloro- or N-trichloroacetylarenesulfonamide determined by titration of a sample in a methanol medium with an alcohol solution of sodium hydroxide.

The results are given in the table.

SUMMARY

1. N-Chloro- and N-trichloroacetylarenesulfonamides are hydrolyzed when boiled in water, dilute acid, or alkali with the formation of arenesulfonamides and chloroacetic or trichloroacetic acid. Under the hydrolysis conditions, the trichloroacetic acid is cleaved with the formation of chloroform and carbon dioxide.

2. N-Trichloroacetylarenesulfonamides are hydrolyzed more rapidly than N-chloroacetylarenesulfonamides.

The introduction of alkyl radicals into the benzene nucleus of N-chloro- and N-trichloroacetylarenesulfonamides slows their hydrolysis.

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REACTION OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

XI. KETOVINYLATION OF METHYLACETYLACETONE AND 2-METHYLDIHYDRORESORCINOL. SYNTHESIS OF UNSATURATED δ-DIKETONES

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As was shown in previous communications, β-chlorovinyl ketones react smoothly with metal derivtives of malonic [1], alkylmalonic [2], and α-alkylacetoacetic esters [3], and esters of cyclic β-keto acids [4] to form normal ketovinylation products.

The studied conversions of the ketovinylation products of β-dicarbonyl compounds obtained showed that they could be used for the synthesis of certain inaccessible classes of substances [5].

Continuing the investigation of ketovinylation, we studied the reaction of β-chlorovinyl ketones with β-diketones. The only example of this reaction was the ketovinylation of 1,4,4-trimethylcyclohexanedione-3,5 (methyldimedone), which we described previously [4]. In view of the fact that the ketovinylation of β-dicarbonyl compounds, which have two labile hydrogen atoms, involves a series of complications [1, 6, 7], we decided to investigate methylacetylacetone, which contains one labile hydrogen atom.

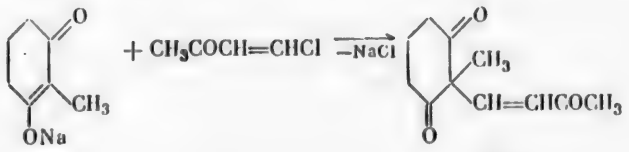
We prepared methylacetylacetone in 50% yield by methylation of acetylacetone with methyl iodide in acetone in the presence of potassium carbonate [8] and then freed it from acetylacetone by washing with 1% sodium hydroxide solution [9]. The reaction of the sodium derivative of methylacetylacetone with β-chlorovinyl ketones in benzene proceeded quite smoothly and the normal ketovinylation products were formed in yields of 44-59%.

$$CH_3C(ONa)=C(CH_3)COCH_3 + RCOCH=CHCl \xrightarrow[-NaCl]{} CH_3COC(CH_3)(CH=CHCOR)COCH_3$$

(I) R = CH_3, (II) R = C_2H_5, (III) R = C_3H_7.

The reaction was carried out under the conditions developed for the ketovinylation of alkylmalonic esters [2] and esters of cyclic β-keto acids [4]. The previously unknown unsaturated triketones obtained as a result of ketovinylation were isolated by distillation at 1-3 mm in a stream of nitrogen after the usual treatment of the reaction mixture. They were yellowish oily substances which were soluble in the usual organic solvents and stable when stored in the cold. Their structure was confirmed by analysis data and the hydrogenation of one of them [methyl-(3-ketobutenyl-1)-acetylacetone], which indicated the presence of one unsaturated bond. The substances obtained were the products of ketovinylation at the carbon as was confirmed by some of their conversions, which will be described below. All these ketovinylation products had a trans configuration.

We also carried out the ketovinylation of 2-methyldihydroresorcinol, which was prepared by the method of I.N. Nazarov and S. I. Zav'yalov [11]. The sodium derivative of 2-methyldihydroresorcinol was prepared in anhydrous methanol, and then the alcohol removed and the ketovinylation performed in dioxane. Ketovinylation with methyl β-chlorovinyl ketone proceeded with difficulty and the bulk of the sodium derivative of 2-methyldihydroresorcinol was recovered from the reaction unchanged even after being boiled in dioxane for 4 hr with 100% excess of methyl β-chlorovinyl ketone.



(IV)

2-Methyl-2-(3'-ketobutenyl-1")-dihydroresorcinol was a colorless, crystalline substance which decomposed quite rapidly on storage; its structure was demonstrated by hydrogenation over palladium on barium sulfate. During the hydrogenation 1 mole of hydrogen was absorbed to form a substance which was identical with that obtained by I. N. Nazarov and S. I. Zav'yalov from the reaction of 2-methyldihydroresorcinol with methyl vinyl ketone [12].

The yields of the ketovinylation products of methylacetylacetone (44-59%) were higher than the yields obtained in ketovinylation of the cyclic β-diketones methyldimedone (37%) [4] and 2-methyldihydroresorcinol (26%) and, as we have established, the ketovinylation of diacetoacetic ester does not occur at all. A comparison of the results of ketovinylation of these β-diketones and esters of β-keto acids [3, 4] with the degree of enolization of these β-dicarbonyl compounds, which is given in the table, shows that the yields of ketovinylation products fall as the degree of enolization increases. The only exception to the rule observed is 1-carbethoxycyclohexanone-2, which is ketovinylated in high yields despite the high degree of enolization (~ 70%) [4]. A similar rule was established by I. N. Nazarov and his co-workers [13] for the condensation of β-dicarbonyl compounds with α,β-unsaturated compounds.

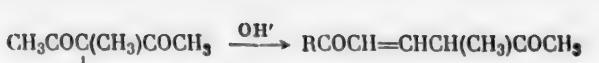
Undoubtedly, the nature of this rule requires thorough study and the degree of enolization may not be the determining, but only an extraneous factor.

In order to study the reactivity of the methyl-(3-ketoalkenyl-1)-acetylacetones obtained by ketovinylation of methylacetylacetone, we treated then with alkali. It was found that under the action of sodium hydroxide these unsaturated triketones smoothly undergo cleavage of a type that is common to β-diketones, to form unsaturated δ-diketones in high yields.

Comparison of the Degree of Enolization of β-Dicarbonyl Compounds• and the Yields of Ketovinylation Products

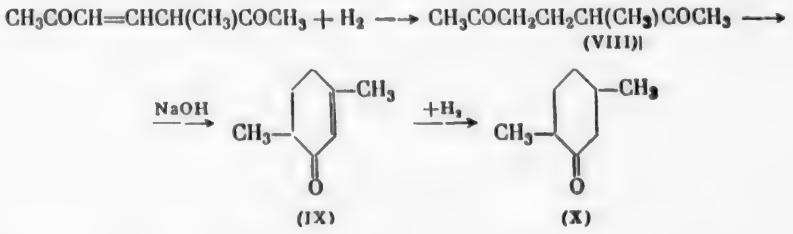
β-Dicarbonyl compound	Degree of enolization (in %)		Yields of ketovinylation products (in %)
	in alcohol	in benzene	
α-Ethylacetoacetic ester	2.8	4.2	55-56
α-n-Butylacetoacetic ester	5.4	6.2	55-66
Carbethoxycyclopentanone	5.9	8.2	64-67
Methylacetylacetone	39.8	–	44-59
Carbethoxycyclohexanone	61.7	74.8	61-65
Methyldihydroresorcinol	93.8	–	25-26
α-Acetylacetoacetic ester	98-100	–	0

•Data on the degree of enolization of β-dicarbonyl compounds were taken from [14].



(V) R = CH_3, (VI) R = C_2H_5, (VII) R = C_3H_7.

These compounds, which were almost inaccessible previously, were yellowish liquids that gradually decomposed during storage. They dissolve in the usual organic solvents and in aqueous solutions of copper acetate or ferric chloride, evidently due to the formation of internal-complex compounds. The structure of the unsaturated δ-diketones was confirmed by analysis data and we also demonstrated it by conversion of 3-methylheptene-4-dione-2,6 to 1,4-dimethylcyclohexanone-2:



(VIII)

(IX) (X)

When 3-methylheptene-4-dione-2,6 was hydrogenated over palladium on barium sulfate, 1 mole of hydrogen was absorbed to form 3-methylheptanedione-2,6, which was cyclized to 1,4-dimethylcyclohexen-1-one-3 by treatment with a 10% aqueous solution of sodium hydroxide at 30°; hydrogenation of this compound over palladium on barium sulfate yielded 1,4-dimethylcyclohexanone-2, which was identified by its boiling point and the melting point of its semicarbazone.

Despite the fact that as yet only methylacetylacetone has been used for investigating the ketovinylation of aliphatic β-diketones and studying the decomposition of the ketovinylation products obtained, there can hardly be any doubt that both these reactions are of a quite general character and may be used as a convenient preparative method for synthesizing the above unsaturated triketones and unsaturated δ-diketones.

EXPERIMENTAL

Methyl-(3-ketobutenyl-1)-acetylacetone (I). Finely divided sodium (6.6 g) was suspended in 100 ml of dry benzene; the benzene was heated to boiling and stirred while 35.7 g of methylacetylacetone was added over a period of 1 hr, and then the reaction mixture was boiled for a further 6-7 hr. The suspension of the sodium derivative obtained was cooled in ice water while a solution of 30 g of methyl β-chlorovinyl ketone in 30 ml of dry benzene was added dropwise over a period of 15-20 min and then the reaction mixture was heated to boiling and boiled for 2-2.5 hr. The benzene solution was washed with water, the wash waters extracted with benzene, which was added to the main portion, and the solvent removed by distillation. The residue was vacuum distilled twice in a stream of nitrogen. The yield was 31 g (59%).

B.p. 100-101° (at 1 mm), d^{20}_4 1.0609, $n^{20}D$ 1.4860, MR_D 49.31; calc. 47.95.

Found %: C 66.27, 66.12; H 7.78, 7.79. $C_{10}H_{14}O_3$. Calculated %: C 65.91; H 7.80.

The yellowish oil was soluble in the usual organic solvents but insoluble in water. It was stable when stored in the cold.

Methyl-(3-ketopentenyl-1)-acetylacetone (II). This compound was obtained analogously from 19 g of methylacetylacetone, 2.2 g of sodium, and 11 g of ethyl β-chlorovinyl ketone in 170 ml of dry benzene. The yield was 8 g (44%).

B.p. 106-107.5° (1 mm), d^{20}_4 1.0400, $n^{20}D$ 1.4822, MR_D 53.81; calc. 52.56

Found %: C 67.56, 67.34; H 8.24, 8.14. $C_{11}H_{16}O_3$. Calculated %: C 67.32; H 8.22.

Methyl-(3-ketohexenyl-1)-acetylacetone (III). This compound was obtained analogously from 28.5 g of methylacetylacetone, 5.3 g of sodium, and 30.5 g of propyl β-chlorovinyl ketone in 380 ml of dry benzene. The yield was 28.5 g (59%).

B.p. 116-118° (1 mm), d^{20}_4 1.0215, $n^{20}D$ 1.4795, MR_D 58.42; calc. 57.18.

Found %: C 68.86, 68.82, H 8.82, 8.76. $C_{12}H_{18}O_3$. Calculated %: C 68.55; H 8.63.

Methyl-(3-ketobutyl-1)-acetylacetone. Methyl-(3-ketobutenyl-1)-acetylacetone (I) (5.9 g) was hydrogenated over 5% Pd/$BaSO_4$ in 60 ml of dry acetone. Hydrogenation stopped completely when 800 ml of hydrogen (18°, 748.5 mm; 785 ml required according to calculation) had been absorbed. After the normal treatment, the residue was vacuum distilled. The yield was 5.6 g (94%).

B.p. 99-102° (1 mm), d^{20}_4 1.0424, $n^{20}D$ 1.4595, MR_D 48.36; calc. 48.41.

Found %: C 65.62, 65.51; H 8.71, 8.58. $C_{10}H_{16}O_3$. Calculated %: C 65.24; H 8.75.

The colorless liquid was soluble in the usual organic solvents.

2-Methyl-2-(3'-ketobutenyl-1')-dihydroresorcinol (IV). To a solution of sodium methylate from 4.2 g of sodium in 80 ml of anhydrous methanol was added a solution of 22.6 g of methyldihydroresorcinol in 50 ml of anhydrous methanol. About 80 ml of alcohol was distilled from the reaction mixture, then 150 ml of dry dioxane was added and distillation continued until the temperature reached 95°. To the reaction mixture, whose volume was about 100 ml, was added a solution of 37.4 g of methyl β-chlorovinyl ketone in 30 ml of dioxane; then the reaction mixture was boiled for 4 hr and cooled to room temperature, and the precipitate collected by filtration and washed with ether; the ether and dioxane were distilled from the filtrate. The residue was kept for 15 min at 20 mm pressure on a bath at 90-95° to remove unreacted methyl β-chlorovinyl ketone and was then treated with ether and the precipitate removed by filtration. The ether was removed and the residue vacuum distilled to yield a fraction with b.p. 147-154° (4 mm). The oil obtained ($n^{20}D$ 1.5182) was crystallized from a very small amount of ether with cooling.

The m.p. was 61-63.5°. The yield was 9 g (26%).

Found %: C 68.26, 68.53; H 7.43, 7.44. $C_{11}H_{14}O_3$. Calculated %: C 68.02; H 7.26.

The colorless crystals decomposed during storage.

2-Methyl-2-(3'-ketobutyl-1')-dihydroresorcinol. 2-Methyl-2-(3'-ketobutenyl-1')-dihydroresorcinol (IV) (4.2 g) was hydrogenated over 5% Pd/$BaSO_4$ in 30 ml of dry acetone. Hydrogenation stopped when 550 ml of hydrogen (15°, 745 mm; 523 ml required according to calculation) had been absorbed. The usual treatment and vacuum distillation yielded 3.9 g of product (92.5%).

B.p. 120-123.5° (0.5-1 mm), $n^{20}D$ 1.4865.

Literature data [12]: b.p. 118-125° (0.1 mm), $n^{20}D$ 1.4910.

Found %: C 67.27, 67.37; H 8.24, 8.32. $C_{11}H_{16}O_3$. Calculated %: C 67.32; H 8.22.

The colorless oily liquid was soluble in the usual organic solvents.

3-Methylheptene-4-dione-2,6 (V). With cooling in ice water and vigorous stirring, 11 g of methyl-(3-ketobutenyl-1)-acetylacetone (I) was added dropwise over a period of 10 min to 65 ml of a 10% solution of NaOH while the reaction mixture temperature was kept at 10-12°, after which stirring was continued for 15-20 min. The alkaline solution was extracted with ether and acidified with 50% H_2SO_4. The oil liberated was separated and the aqueous layer carefully extracted with ether. The ether extracts were added to the bulk of the substance and dried with magnesium sulfate. After removal of the solvent, the residue was vacuum distilled in a stream of nitrogen. The yield was 6.5 g (76.5%).

B.p. 74-75.5° (1 mm), d^{20}_4 0.9979, $n^{20}D$ 1.4756, MR_D 39.59; calc. 38.70.

Found %: C 68.22, 68.45; H 8.52; 8.62 $C_8H_{12}O_2$. Calculated %: C 68.54; H 8.63.

The yellowish oil was soluble in the usual organic solvents but insoluble in water. It gradually resinified during storage.

3-Methyloctene-4-dione-2,6 (VI). This compound was obtained analogously from 7.1 g of methyl-(3-ketopentenyl-1)-acetylacetone (II) by treatment with 40 ml of 10% NaOH solution. The yield was 4.3 g (76.5%).

B.p. 82-83° (1 mm), d^{20}_4 0.9809, $n^{20}D$ 1.4743, MR_D 44.24; calc. 43.32.

Found %: C 69.92; H 9.38. $C_9H_{13}O_2$. Calculated %: C 70.10; H 9.15.

3-Methylnonene-4-dione-2,6 (VII). This compound was obtained analogously by treating 10 g of methyl-(3-ketohexenyl-1)-acetylacetone (III) with 55 ml of 10% NaOH solution. The yield was 6.5 g (81.5%).

B.p. 87-88.5° (1 mm), d^{20}_4 0.9648, $n^{20}D$ 1.4725, MR_D 48.86; calc. 47.94.

Found %: C 71.22, 71.44; H 9.60, 9.89. $C_{10}H_{16}O_2$. Calculated %: C 71.39, H 9.59.

3-Methylheptanedione-2,6 (VIII). 3-Methylheptene-4-dione-2,6 (V) (9.5 g) was hydrogenated in 40 ml of dry acetone over $Pd/BaSO_4$. Hydrogenation stopped completely when 1690 ml of hydrogen (1612 ml according to calculation) had been absorbed. After the usual treatment, the residue was vacuum distilled. The yield was 9 g (94%).

B.p. 79-80.5° (5 mm), d^{20}_4 0.9497, $n^{20}D$ 1.4353, MR_D 39.09; calc. 39.17.

Found %: C 67.71, 67.74; H 10.17, 10.18. $C_8H_{14}O_2$. Calculated %: C 67.57; H 9.92.

The disemicarbazone formed colorless crystals with m.p. 175-176° (from 30% alcohol).

1,4-Dimethylcyclohexene-1-one-3 (IX). 3-Methylheptanedione-2,6 (VIII) (3.6 g) was stirred with 18 ml of 10% NaOH solution at 30° for 10 min. The oil liberated was separated and the aqueous layer extracted with ether. The ether extracts were combined with the main part of the oil and dried with calcium chloride. After removal of the ether, the residue was vacuum distilled. The yield was 2.2 g (70%).

B.p. 76-78° (8 mm), d^{20}_4 0.9521, $n^{20}D$ 1.4867.

Found %: C 77.17; H 9.75. $C_8H_{12}O$. Calculated %: C 77.38; H 9.74.

The colorless liquid had a characteristic smell.

1,4-Dimethylcyclohexanone-2 (X). 1,4-Dimethylcyclohexene-1-one-3 (IX) (1.9 g) was hydrogenated in 95 ml of dry acetone over $Pd/BaSO_4$. Hydrogenation stopped when 370 ml of hydrogen (373 ml according to calculation) had been absorbed. After the usual treatment, the residue was vacuum distilled.

B.p. 176-177° (745 mm), 65-68° (15 mm), $n^{20}D$ 1.4460. Literature data: b.p. 174-177° [15]; 178°, $n^{20}D$ 1.4446 [16].

The semicarbazone formed colorless crystals with m.p. 166-166.5° (from 30% alcohol).

Found %: N 23.16. $C_9H_{17}N_3O$. Calculated %: N 22.93.

Literature data: m.p. 167° [15], 175-176° [16], 170° [17], 155° [18].

SUMMARY

1. The reaction of β-chlorovinyl ketones with the sodium derivatives of methylacetylacetone and 2-methyldihydroresorcinol yielded methyl-(3-ketoalkenyl-1)-acetylacetones and 2-methyl-2-(3'-ketobutenyl-1')-dihydroresorcinol, which were previously unknown.

2. Treatment of methyl-(3-ketoalkenyl-1)-acetylacetones with an aqueous solution of sodium hydroxide gave high yields of unsaturated δ-diketones.

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INVESTIGATIONS ON THE ISOXAZOLE SERIES

IX. SYNTHESIS OF 3-SUBSTITUTED ISOXAZOLES. CLEAVAGE OF ISOXAZOLES WITH SODAMIDE

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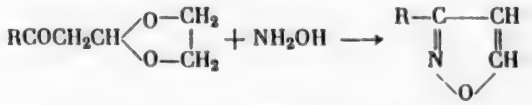
The most convenient of the known methods of synthesizing monosubstituted isoxazoles, which are based on the condensation of hydroxylamine with β-dicarbonyl compounds (oxymethylene ketones [1], β-chlorovinyl ketones [2], etc.), lead to a mixture of 3- and 5-substituted isomers whose separation involves considerable difficulties and is sometimes impossible. In this connection, the development of general methods for synthesizing monosubstituted isoxazoles which give only one of the isomers is of considerable interest. This problem has been solved for 5-substituted isoxazoles by starting from β-dialkylaminovinyl ketones, which condense with hydroxylamine hydrochloride to give only 5-substituted isomers [3,4]. Up to now there has been no general method of synthesizing 3-substituted isoxazoles. The method based on the reduction of 3-α-haloalkylisoxazoles [5] is only of limited value.

We developed a synthesis which makes it possible to prepare selectively 3-substituted isoxazoles and which consists of the reaction of hydroxylamine as the base with ethylene glycol acetals of β-keto aldehydes (ω-acylmethyldioxalans). As is known [6], the condensation of dialkyl acetals of β-keto aldehydes with hydroxylamine hydrochloride also forms a mixture of 3- and 5-substituted isomers. On the basis of the fact that a cyclic acetal grouping is considerably more stable than a dialkyl acetal grouping, we attempted to prepare 3-substituted isoxazoles by the reaction of ethylene glycol acetals of β-keto aldehydes, for which a convenient synthesis method was recently developed [7]. However, condensation of ethylene glycol acetals of β-keto aldehydes with hydroxylamine hydrochloride in alcohol again gave only a mixture of isomers, which was undoubtedly connected with preliminary hydrolytic cleavage of the acetal grouping in the acid medium and subsequent reaction of the β-keto aldehyde formed in both possible directions.

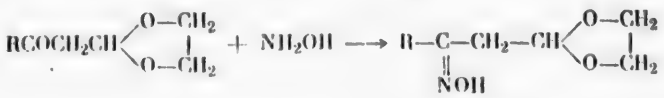
A different result was obtained by condensation of ethylene glycol acetals of β-keto aldehydes with hydroxylamine as the base. In order to eliminate possible transacetalation and the formation of the less stable dialkyl acetal [7], the reaction was carried out not in alcohol, but in aqueous dioxane. In this case the reaction proceeded unequivocally and led to pure 3-substituted isoxazoles, which did not contain even traces of the 5-substituted isomers.



(I) R = C_3H_7; (II) R = iso-C_4H_9; (III) R = C_6H_5.

This method gave good yields of both 3-alkylisoxazoles and 3-phenylisoxazole. Due to its simplicity and the accessibility of the starting materials, this method is the most convenient one for the synthesis of 3-substituted isoxazoles.

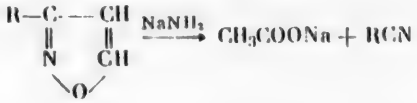
On the example of 3-phenylisoxazole preparation, it was possible to show that the reaction proceeds through the intermediate formation of the oxime of the ethylene glycol acetal of the β-keto aldehyde, which spontaneously cyclizes to 3-phenylisoxazole with further heating.



(IV)

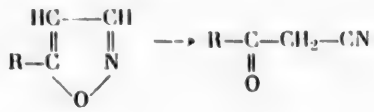
The cyclization proceeds much more readily in an acid medium, as the cyclic acetal grouping is then hydrolyzed more readily. From the preparative point of view, the reaction is carried out most conveniently without isolation of the oxime by direct heating of the acetal and hydroxylamine as the base for 20-25 hr.

The structure and purity of the compounds obtained were demonstrated by their cleavage reactions. When the isoxazoles obtained were treated in the cold with an alcohol solution of sodium alcoholate by Claisen's method [8], not even traces of the corresponding β-keto nitriles were liberated, indicating that the isomeric 5-substituted isoxazoles were completely absent from the preparations obtained. As is known [8], 3-substituted isoxazoles are decomposed under the action of alcoholate according to a different scheme and under much more drastic conditions and the isolation and identification of their decomposition products, sodium acetate and a nitrile, is often extremely difficult. We attempted to find a more convenient method of cleaving the nucleus of 3-substituted isoxazoles, which was necessary for demonstrating the structure of the compounds we obtained and which would be suitable for 3-substituted isoxazoles in general. In this connection we studied the reaction of 3-substituted isoxazoles with sodamide in xylene. Considering the close analogy in the behavior of isoxazoles and pyridines [9], one might have expected direct amination by a Chichibabin reaction. However, instead of this there was decomposition of the isoxazole ring with the formation of sodium acetate and a nitrile, similar to the case of drastic treatment with alcoholate [8].



Evidently, the well-known sensitivity of the isoxazole nucleus to nucleophilic agents is the deciding factor in this case and makes nucleophilic substitution in the nucleus impossible. The decomposition reaction proceeded extremely smoothly, the decomposition products were readily identified, and the reaction may be recommended for the identification and demonstration of the structure of 3-substituted isoxazoles instead of the less convenient method involving drastic treatment with alcoholate.

As was to be expected, 5-substituted isoxazoles, which are even more sensitive to nucleophilic agents, also underwent ring opening under the action of sodamide to form the corresponding β-keto nitriles (5-phenylisoxazole gave a quantitative yield of ω-cyanoacetophenone). However, in this case the reaction has no advantages over the well-known cleavage of 5-substituted isoxazoles by an alcohol solution of sodium alcoholate in the cold by Claisen's method [8].



EXPERIMENTAL

3-Phenylisoxazole (III). To a solution of 10 g of ω-benzoylmethyldioxalan [1] in 50 ml of aqueous dioxane (3 : 1) was added an aqueous solution of 5.4 g of hydroxylamine hydrochloride adjusted to a neutral reaction with potassium carbonate and the reaction mixture left at room temperature for two days, when it was heated on a boiling water bath for 20 hr. The cooled reaction mixture was poured into water, the liberated oil separated, and the aqueous layer extracted with ether. The combined substances and extracts were dried over $MgSO_4$, the ether removed and the residue vacuum distilled. The yield was 4.9 g (65%).

B.p. 89-90° (2 mm), $n^{20}D$ 1.5735, d^{20}_4 1.1408.

Found %: C 74.55, 74.63; H 5.05, 5.19. C_9H_7ON. Calculated %: C 74.58; H 4.82.

A sample (1.534 g) of the substance obtained was dissolved in anhydrous alcohol and heated with a solution of 0.243 g of sodium in anhydrous alcohol. When the reaction mixture was poured into water and acidified, not even traces of ω-cyanoacetophenone were formed.

3-Phenyl-2-methylisoxazolium chloroferrate. A sample (0.5 g) of the substance and 1.5 ml of freshly distilled dimethyl sufate were heated on a water bath for 3 hr. To the cooled reaction mixture was added 5 ml of HCl (1 : 1) and after 30 min, 5 ml of a concentrated solution of $FeCl_3$ (2 parts of $FeCl_3 \cdot 6H_2O$ to 1 part of H_2O). The yellow precipitate was collected by filtration and dried in vacuum over P_2O_5. The yield was 1.05 g (85%). The yellow crystals had m.p. 77-78° (from glacial acetic acid).

Found %: C 33.77, 33.79; H 2.95, 3.01. $C_{10}H_9ONCl_4Fe$. Calculated %: C 33.54, H 2.79.

3-Propylisoxazole (I) was obtained analogously from 7.2 g of propionylmethyldioxalan [1] in 30 ml of dioxane and 3.2 g of hydroxylamine hydrochloride neutralized with potassium carbonate. The yield was 3 g (67%).

B.p. 74-75° (40 mm), $n^{20}D$ 1.4435. Literature data for 5-propylisoxazole [2]: b.p. 160-161.5°, $n^{20}D$ 1.4460.

When the substance obtained was treated with an alcohol solution of sodium ethylate, none of the sodium derivative of cyanomethyl propyl ketone was formed.

3-Isobutylisoxazole (II) was obtained analogously from 10 g of isovaleryldioxalan [1] in 50 ml of methanol and 6 g of hydroxylamine hydrochloride neutralized with potassium carbonate. The yield was 5 g (77%).

B.p. 81-82° (30 mm), $n^{20}D$ 1.4443. Literature data for 5-isobutylisoxazole [2]: b.p. 168-169° (760 mm) $n^{20}D$ 1.4480.

Treatment of the substance obtained with an alcohol solution of sodium ethylate did not form any of sodium derivative of cyanomethyl isobutyl ketone.

ω-Benzoylmethyldioxalan oxime (IV, R = C_6H_5). To a solution of 17.7 g of ω-benzoylmethyldioxalan in 75 ml of aqueous dioxane (3 : 1) was added an aqueous solution of 10.6 g of hydroxylamine hydrochloride neutralized with potassium carbonate. The reaction mixture was heated on a water bath for 7 hr, cooled and poured into water. We obtained 12 g (63%) of colorless crystals with m.p. 110-111° (from aqueous alcohol).

Found %: N 6.63, 6.49. $C_{11}H_{13}O_3N$. Calculated %: N 6.76.

3-Phenylisoxazole (III) by cyclization of the oxime. A. A sample (7 g) of oxime was dissolved in aqueous dioxane and boiled for 12 hr. The reaction mixture was cooled and poured into water and the liberated oil extracted with ether and dried with $MgSO_4$. Distillation yielded 3.18 g of product (60%). It had b.p. 95-96° (3 mm), $n^{20}D$ 1.5700.

B. A sample (5 g) of oxime was dissolved in aqueous dioxane and the solution made acid to Congo with hydrochloric acid and heated on a water bath for 1 hr. The reaction mixture was treated as described above to yield 2.2 g of product (63%). It had b.p. 95-96° (3 mm), $n^{20}D$ 1.5703.

No ω-cyanoacetophenone was formed when the substance obtained by either method was treated with sodium ethylate solution.

The chloroferrate, which was obtained as described above, formed yellow crystals with m.p. 77-78°. A mixed melting point with a sample obtained directly from ω-benzoylmethyldioxalan was not depressed.

Cleavage of isoxazoles with sodamide. 3-Phenylisoxazole. A sample (3 g) of (III) was dissolved in 7 ml of dry xylene and 0.85 g of powdered $NaNH_2$ added. The reaction mixture was heated on a water bath for 2 hr. This precipitated CH_3COONa (1.6 g, 94%), which was collected and converted into the p-bromophenacyl ester with m.p. 84-85°. Literature data [3]: m.p. 85°. The xylene was distilled from the filtrate and the residue vacuum distilled. We obtained 1.5 g (70%) of C_6H_5CN with b.p. 100-105° (40 mm), which was hydrolyzed with sodium hydroxide solution with heating and converted into benzoic acid with m.p. 121-121.5°; a mixed melting point with an authentic sample was not depressed.

3-Propylisoxazole. To a solution of 2 g of (I) in 10 ml of dry xylene was added 0.78 g of powdered $NaNH_2$ and the reaction mixture heated at 100-120° for 1.5 hr. The crystals liberated were collected to yield 1.4 g (95%) of CH_3COONa. The p-bromophenacyl ester prepared from the sodium acetate obtained had m.p. 84-85°. To the filtrate, which contained butyronitrile, were added 20 ml of absolute ether, 1.3 g of phloroglucinol, and 0.7 g of $ZnCl_2$ and then a strong stream of HCl was passed in at room temperature for 30 min. The oil which was liberated was dissolved in water and the aqueous solution washed with ether and evaporated to $\frac{1}{3}$ of its volume. The precipitate which formed on cooling was collected to yield yellow crystals with m.p. 180-181° (from water). Literature data for phloropropiophenone [4]: m.p; 180-181°.

3-Methylisoxazole. A sample (3.5 g) of 3-methylisoxazole was treated analogously with 1.7 g of $NaNH_2$ in 10 ml of dry xylene. The CH_3COONa was collected and identified and the filtrate treated with phloroglucinol, $ZnCl_2$, and alcoholic HCl to yield yellow crystals with m.p. 218-220° (from water). Literature data for phloroacetophenone [5]: m.p. 218-219°.

5-Phenylisoxazole. A sample (2 g) of 5-phenylisoxazole was dissolved in 5 ml of dry xylene and 0.7 g of $NaNH_2$ added. The white, crystalline precipitate was collected to give 2.3 g of the sodium derivative of ω-cyanoacetophenone (quantitative yield). The crystals obtained were dissolved in water and the solution acidified to Congo with HCl and extracted with ether. The ether was evaporated in the cold to yield ω-cyanoacetophenone with m.p. 80-81°. Literature data [6]: m.p. 80-81°. A mixed melting point with an authentic sample was not depressed.

SUMMARY

1. A method was developed for synthesizing 3-substituted isoxazoles by condensation of ethylene glycol acetals of β-keto aldehydes (ω-acylmethyldioxalans) with hydroxylamine as the base in aqueous dioxane. The yields were 65-80%.

2. It was shown that under the action of sodamide, 3-substituted isoxazoles are cleaved with the formation of sodium acetate and the corresponding nitrile. This reaction is recommended for demonstrating the structure and identifying 3-substituted isoxazoles.

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VINYLATION OF ETHYLENE GLYCOL MONOETHERS

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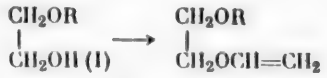
The vinylation of ethylene glycol by the Favorskii-Shostakovskii method and the investigation of the products obtained have been described in detail [1]. Meanwhile, the vinylation of monoethers of ethylene glycol has not been studied adequately [2]. There is a report on the vinylation of the monobutyl ether of ethylene glycol, but the constants were not given [3].

It seemed interesting to synthesize monoethers of ethylene glycol with an allyl radical and to find conditions for their vinylation.



(I) $R=C_4H_9$,
(II) $R=CH_3CH=CHCH_2$,
(III) $R=CH_2=CHCH(CH_3)$.

The vinyl butyl, vinyl crotyl, and vinyl α-methylallyl ethers of ethylene glycol were mobile liquids with a characteristic ether smell. Their structure and the presence of double bonds in them were demonstrated by hydrolytic oximation and hydrogenation over Raney nickel. Hydrogenation yielded saturated ethers of ethylene glycol, which have been described in the literature [4].

EXPERIMENTAL

Monobutyl, monocrotyl, and mono-α-methylallyl ethers of ethylene glycol. To 500 g of ethylene glycol heated to 50° was added 70 g of metallic sodium in portions with stirring. When all the sodium had dissolved, the mixture was heated on a water bath while the alkyl halide (300 g of butyl chloride or 430 g of a mixture of crotyl and α-methylallyl bromides) was added slowly. After 3-4 hr, the reaction mixture was filtered to remove sodium chloride and vacuum distilled.

a) We obtained 220 g (61%) of the monobutyl ether of ethylene glycol.

B.p. 78-80° (22 mm), d^{20}_4 0.8981, $n^{20}D$ 1.4197, MR_D 33.27; calc. 33.07.

b) We obtained 285 g (75%) of a mixture of crotyl and α-methylallyl ethers of ethylene glycol; 57 g (17.6%) of α-methylallyl ether of ethylene glycol.

B.p. 68-70° (20-21 mm), d^{20}_4 0.9147, $n^{20}D$ 1.4310, MR_D 32.87; calc. 32.61.

Found %: C 62.40, 62.10; H 10.25, 10.22. M 117.5. $C_6H_{12}O_2$. Calculated %: C 62.03; H 10.41. M 116.2.

105 g (27.6%) of monocrotyl ether of ethylene glycol.

B.p. 85-87° (21-22 mm), d^{20}_4 0.9387, $n^{20}D$ 1.4428, MR_D 32.78; calc. 32.61.

Found %: C 62.21, 61.89; H 10.31, 10.21. M 118.3. $C_6H_{12}O_2$. Calculated %: C 62.03; H 10.41. M 116.2.

Vinyl butyl and vinyl crotyl ethers of ethylene glycol. The monoethers of ethylene glycol were placed in an autoclave with 10% potassium hydroxide. The acetylene pressure in the tank was 18 atm. Vinylation was carried out at 150° for 4 hr. The maximum pressure in the autoclave was 45 atm. The product was washed from the autoclave with ether. The ether solution was washed carefully with water and then dried with potassium carbonate. The ether was removed and the residue vacuum distilled.

a) Vinylation of 30 g of the monobutyl ether of ethylene glycol yielded 25.4 g (70%) of the vinyl butyl ether of ethylene glycol.

B.p. 70-72° (20-21 mm), d^{20}_4 0.8658, $n^{20}D$ 1.4213, MR_D 42.26; calc. 41.96.

Found %: C 66.51, 66.55; H 10.88, 10.85. M 143.0. $C_8H_{16}O_2$. Calculated %: C 66.62; H 11.18. M 114.2.

Found %: acetaldehyde 97.4, 97.9.

b) Vinylation of 30.7 g of the monocrotyl ether of ethylene glycol yielded 22.1 g (59%) of the vinyl crotyl ether of ethylene glycol.

B.p. 77-80° (21-22 mm), d^{20}_4 0.8958, $n^{20}D$ 1.4410, MR_D 41.88; calc. 41.49.

Found %: C 67.48, 67.66; H 9.61, 9.60. M 144.4. $C_8H_{14}O_2$. Calculated %: C 67.57; H 9.92. M 142.2.

Found %: acetaldehyde 99.5, 99.3.

Vinyl α-methylallyl ether of ethylene glycol. In 30.7 g of the α-methylallyl ether of ethylene glycol was dissolved 0.5 g of metallic potassium (10% alcoholate). The mixture was placed in an autoclave and vinylated at 150° for 3 hr. The product was treated as described above. We obtained 26 g (69%) of the vinyl α-methylallyl ether of ethylene glycol.

B.p. 72-74° (36 mm), d^{20}_4 0.8761, $n^{20}D$ 1.4300, MR_D 41.92; calc. 41.49.

Found %: C 67.87, 67.93; H 9.79, 9.75. M 141.1. $C_8H_{14}O_2$. Calculated %: C 67.57; H 9.92. M 142.2.

Found %: acetaldehyde 99.3, 100.2.

The hydrogenation of vinyl ethers of ethylene glycol was carried out in alcohol over Raney nickel with vigorous shaking.

a) When 2.1 g of the vinyl butyl ether of ethylene glycol was hydrogenated, 353 ml of hydrogen (101%) was absorbed in 2 hr. We obtained 1.3 g (62%) of the ethyl butyl ether of ethylene glycol.

B.p. 68-69° (24-25 mm), d^{20}_4 0.8414, $n^{20}D$ 1.4055, MR_D 42.64; calc. 42.43.

Found %: C 65.41, 65.47; H 12.06, 12.04. $C_8H_{18}O_2$. Calculated %: C 65.70; H 12.40.

b) When 2.1 g of the vinyl crotyl ether of ethylene glycol was hydrogenated, 726 ml of hydrogen (101%) was absorbed in 2 hr. We obtained 1.8 g (81%) of the ethyl butyl ether of ethylene glycol.

B.p. 59-61° (17 mm), d^{20}_4 0.8426, $n^{20}D$ 1.4060, MR_D 42.68; calc. 42.43.

c) When 3.5 g of the vinyl α-methylallyl ether of ethylene glycol was hydrogenated, 1200 ml of hydrogen (107%) was absorbed in 3 hr. We obtained 2.65 g (75%) of the ethyl sec-butyl ether of ethylene glycol.

B.p. 69-71° (37-38 mm), d^{20}_4 0.8327, $n^{20}D$ 1.4026, MR_D 42.81; calc. 42.43.

Found %: C 65.94, 65.77; H 12.11, 12.27. M 143.7. $C_8H_{18}O_2$. Calculated %: C 65.70; H 12.40. M 146.2.

SUMMARY

1. The crotyl and α-methylallyl ethers of ethylene glycol were prepared and characterized.

2. Vinylation of the butyl, crotyl, and α-methylallyl ethers of ethylene glycol yielded the vinyl butyl, vinyl crotyl, and vinyl α-methylallyl ethers of ethylene glycol.

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ORGANOMAGNESIUM SYNTHESIS OF 2-OCTYLBUTADIENE-1,3

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1,3-Butadienes with various substituents at C_2 may be prepared by the general method proposed by Carothers [1], which consists of reacting 4-chlorobutadiene-1,2 (I) with alkyl(aryl)magnesium halides to form two types of product, namely, "normal" $CH_2 = C = CH-CH_2R$ (A) and "anomalous" $CH_2 = CR-CH = CH_2$ (B).

The purpose of the present work was to prepare 2-octylbutadiene-1,3 by Carothers' method. From the reaction mixture obtained by reaction of octylmagnesium bromide (II) with an equivalent amount of 4-chlorobutadiene-1,2 (I), we isolated 2-octylbutadiene-1,3 (III), hexadecane (IV), and octatetrene (V); 4-octylbutadiene-1,2, whose formation was also possible, was only present as a trace. In six experiments the reaction of 1.71 mole of (I) with 1.74 mole of (II) gave 0.6 mole of (III), 0.44 mole of (IV), and 0.36 mole of (V). The yields were 34.3, 50.3, and 41 mol. %, respectively. Thus, the molar percent utilization of (I) was 75.3 and of (II), 84.6. The formation of octatetrene was unexpected as there are no reports on this in the work of Carothers and other investigators who used 4-chlorobutadiene-1,2 in organomagnesium synthesis, probably because it polymerizes extremely readily during vacuum distillation.

In connection with the results we obtained, it is appropriate to make a few observations on the mechanism of the reaction of 4-chlorobutadiene-1,2 with alkylmagnesium halides. Carothers [2] rejected the hypothesis of radical or ionic mechanisms and suggested that the formation of both types of product may be explained by the existence of an unstable linear internal complex involving 4-chlorobutadiene-1,2, the alkylmagnesium halide, and ether. While he pointed out yet another possible reaction mechanism through the addition of RMgX at the double bond with subsequent elimination of MgX_2, Carothers did not analyze this as at that time there were no known cases of the addition of RMgX to a C = C bond. Such reactions are known at the present time. Thus, in an investigation of the reaction of ethylmagnesium bromide with 1,2-heptadiene-3-carboxylic acid, Wotiz [3] isolated 2-ethyl-1-heptene-3-carboxylic acid which, in his opinion, could have been formed by addition of C_2H_5MgBr at the double bond both in the 3,4- and 1,4-positions. The addition of RMgX to a double bond has been demonstrated in the case of bis-(diphenylene)-ethylene [4]. Addition of the Grignard reagent to 4-chlorobutadiene-1,2 at the double bond may explain the formation of the "anomalous" product but not the "normal" product. It seems to us that the formation of both these products occurs in two stages: An unstable transition complex is first formed and this then rearranges to quite stable cyclic complexes as a result of interaction through the C = C bond or with transfer of the reaction center along the conjugation chain. Monomolecular decomposition of such compounds leads to the formation of 4-alkylbutadiene-1,2 or 2-alkylbutadiene-1,3. Reaction of the complex compounds with each other leads to products of the R-R type and octatetrene.

EXPERIMENTAL

Condensation of octylmagnesium bromide with 4-chlorobutadiene-1,2. A solution of octylmagnesium bromide, prepared in the usual way (from 7.5 g of magnesium ribbon and 51 g of octyl bromide in 200 ml of absolute ether), was passed through a No. 2 glass filter into a second flask. The undissolved residue of magnesium

was removed from the first flask and found to weight 1.25 g . A solution of 23 g of 4-chlorobutadiene-1,2 in 100 ml of absolute ether was added over 1 hr with stirring to the octylmagnesium bromide solution. When almost the whole of the chlorobutadiene had been added, in a period of 1-2 min the reaction mixture changed to a white, pasty mass. The flask was heated on a water bath with the ether boiling gently for a further 2 hr and then cooled and the contents poured into a mixtureof ice and 10% NH_4Cl solution. The ether layer was separated, washed with water, and dried over $CaCl_2$ and the ether removed on a water bath. The residue (35.2 g) was vacuum distilled on a column. Three fractions were obtained.

Investigation of 1st fraction. After redistillation in vacuum, the fraction had b.p. 28-30° (50 mm), $n^{20}D$ 1.4380, d^{20}_4 0.8438. The colorless, volatile liquid rapidly became turbid in air; an ether-insoluble precipitate gradually formed. The precipitate was collected and washed with ether, when it exploded violently on contact and was evidently a peroxide.

Bromide. The 1st fraction was brominated at 0° in $CHCl_3$. After removal of the excess bromine and evaporation of the chloroform, the solid residue was recrystallized from alcohol. The slightly yellowish needles had m.p. 127-129° (in a sealed capillary).

Found %: C 15.15; H 2.08; Br 80.90. $C_8H_{10}Br_8 \cdot C_2H_5OH$. Calculated %: C 15.15; H 2.02; Br 80.81.

The first fraction was probably the octatetrene $CH_2 = C = CH-CH_2-CH_2-CH = C = CH_2$.

Investigation of 2nd fraction. After redistillation in vacuum on a column, it had b.p. 70-77° (5 mm), $n^{20}D$ 1.4522 (first distillate) and 1.4530 (later distillate), d^{20}_4 0.8924.

Found %: C 86.40; H 13.80. $C_{12}H_{22}$. Calculated %: C 86.75; H 13.25.

The bromide obtained could not be crystallized and purified for analysis.

Adduct with maleic anhydride. A sample (1.7 g) of the substance was heated with 1 g of maleic anhydride and 10 ml of benzene in a sealed ampoule for 4 hr at 95°. The ampoule was opened, the benzene solution evaporated, and the solid residue recrystallized twice from ligroin. The yield was 1.8 g (74%). After purification by heating with water, the adduct was dried in vacuum over P_2O_5; it had m.p. 48.5-49°.

Found %: C 73.05, 72.99; H 8.80, 9.21. $C_{16}H_{24}O_3$. Calculated %: C 72.72; H 9.09.

The 2nd fraction was 2-octylbutadiene-1,3. The difference in refractive indices between the first and subsequent distillates indicates the presence of some impurity, probably 4-octylbutadiene-1,2.

Investigation of 3rd fraction. After redistillation in vacuum, the fraction had b.p. 109-110° (1.5 mm) and crystallized at room temperature. Hexadecane has b.p. 110° (1 mm) and m.p. 19-20°.

SUMMARY

1. The reaction of 4-chlorobutadiene-1,2 with octylmagnesium bromide was studied. We isolated the previously undescribed 2-octylbutadiene-1,3, which was characterized as the adduct with maleic anhydride, and an octatetrene C_8H_{10}, which was characterized as the octabromide.

2. A scheme is proposed for the reaction between 4-chlorobutadiene-1,2 and alkylmagnesium halides through the formation and decomposition of complexes.

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SYNTHESIS AND CONVERSIONS OF ar-β- AND ac-β-TETRALYL PHENYL SULFIDES• ON AN ALUMINOSILICATE CATALYST

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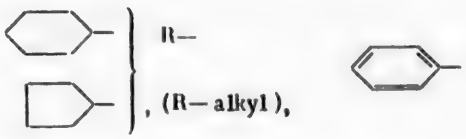
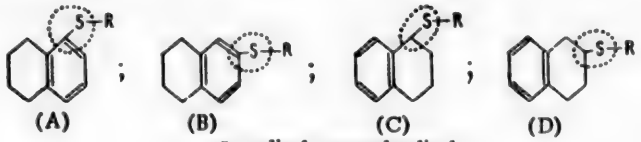
In previous work [1, 2] it was shown that in contact with an aluminosilicate catalyst at 300°, molecules of mixed sulfides decompose with rupture of one of the bonds of sulfur with the radicals. From the structure of the substances isolated from the catalyzates it is possible to determine the position at which the molecule was ruptured. A comparison of the data obtained made it possible to draw conclusions on the strength of the bonds of sulfur with different radicals. It was established that the bond of sulfur with a benzene ring is strongest, the bond of sulfur with naphthene radicals (cyclopentyl and cyclohexyl) is weakest, and the bond between sulfur and alkyls occupies an intermediate position with respect to strength. For clarity we give a series arranged with respect to increasing strength of the bond of sulfur with the radicals.



A study of the conversions of mixed α-(ar- and ac-) and β-(ar- and ac-) sulfides of tetralin on an aluminosilicate catalyst at 300° showed that both rings of the condensed system of tetralin have a weakening action on the bond of sulfur with the second ring of tetralin [3]. Thus, the bonds ringed with a broken line in compounds of type (A) and (B) are considerably weaker



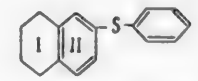
R= alkyl or cycloalkyl

than the bond in the one-ring systems (a) and the bonds in compounds (C) and (D) are weaker than those in compounds of type (b).

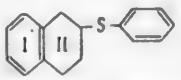
R= alkyl or cycloalkyl R = cycloalkyl

•The symbols ar and ac denote that the substituent is in the benzene or hexamethylene ring of the tetralin, respectively.

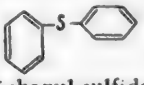
The purpose of the present work was to confirm the mutual weakening effect of one ring of tetralin on the bond of sulfur with tetralin in the other ring when the second radical of the mixed sulfide is phenyl. For this purpose we synthesized two sulfides of the tetralin series, namely, ar-β-tetralyl phenyl sulfide and ac-β-tetralyl phenyl sulfide.



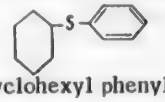
ar-β-tetralyl phenyl sulfide



ac-β-tetralyl phenyl sulfide

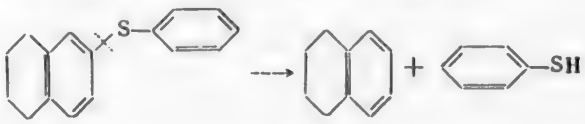


diphenyl sulfide



cyclohexyl phenyl sulfide

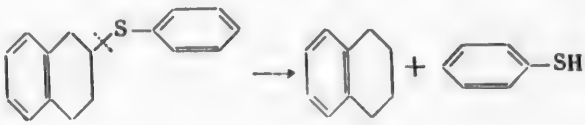
These compounds may be compared with diphenyl sulfide and cyclohexyl phenyl sulfide. The former differ from the latter in the presence of the second condensed ring. In diphenyl sulfide the two bonds of sulfur with the benzene nuclei are equivalent. Considering the weakening action of the hexamethylene ring (I) of ar-β-tetralyl phenyl sulfide on the bond between the sulfur and the benzene ring (II) of tetralin, we expected rupture at precisely this point in the molecule with the formation of tetralin and thiophenol.



(1)

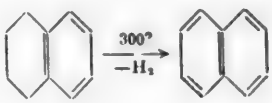
The hydrogen needed for the reaction would be formed by disproportionation on the aluminosilicate.

As we observed previously [1], in cyclohexyl phenyl sulfide the bond of sulfur with the hexamethylene ring is much weaker than the bond of sulfur with the aromatic ring and breaks when this sulfide is in contact with aluminosilicate. Considering the weakening effect of the aromatic ring (I) of ac-β-tetralyl phenyl sulfide on the bond of sulfur with the hexamethylene ring (II) of tetralin, we were certain that the latter bond would break with the formation of tetralin and thiophenol, i.e., the reaction would occur according to scheme (2).



(2)

Passing ar-β-tetralyl phenyl sulfide over an aluminosilicate catalyst at 300° yielded a catalyzate from which we isolated thiophenol (37% of the catalyzate weight), tetralin (33%), and naphthalene (8%). Only 1.3% of the sulfur of the original sulfide was trapped in the form of hydrogen sulfide. These data indicate that rupture of the molecule of ar-β-tetralyl phenyl sulfide actually occurred between the sulfur and the tetralin ring according to scheme (I) with the formation of thiophenol and tetralin. The effect of the hexamethylene ring was found to be so great that it considerable changed the ratio of the strengths of the bonds of sulfur with the aromatic nuclei and made the process occur in one direction only. The presence of naphthalene in the catalyzate is explained by a secondary process, namely, dehydrogenation of the hexamethylene ring of tetralin.



(3)

We observed this reaction previously [4].

The catalyzate obtained by passing ac-β-tetralyl phenyl sulfide over aluminosilicate at 300° yielded thiophenol (42% of the catalyzate weight), tetralin (20%), and naphthalene (11%). Consequently, the results of catalysis again confirm scheme (2). The sulfide decomposed to thiophenol and tetralin. The formation of naphthalene was a secondary process and occurred according to scheme (3).

The study of the conversions of isomeric ar-β- and ac-β-tetralyl phenyl sulfides on aluminosilicate thus confirmed the weakening action of one ring of tetralin on the bond of sulfur with the other ring, which we disco-

vered previously. In both cases rupture of the sulfide molecule actually occurred at the bond of sulfur with the tetralin nucleus, regardless of whether the sulfur was in this nucleus in the ar-β - or ac-β position.

EXPERIMENTAL

ar-β -Tetralyl phenyl sulfide was synthesized by the diazo method [5]. Into a beaker fitted with a stirrer was placed 33.6 g of KOH, 100 ml of alcohol added, and the mixture heated on a water bath to 70-75°. When a homogeneous solution had been formed, 49.2 g of ar-β -thiotetralol [4] was introduced into the beaker and with continuous stirring, a solution of benzenediazonium chloride,* prepared in the usual way from 27.9 g of aniline, was added in small portions. The addition of the diazo solution was stopped when the yellow precipitate which formed during the reaction turned appreciably brown. The reaction mixture was heated on a water bath until the evolution of nitrogen ceased; then the brown oil liberated was separated, the aqueous layer extracted with ether, and the ether extract combined with the oil. The ether solution was washed free from alkali with water and dried with calcium chloride. The sulfide was vacuum distilled twice over metallic sodium. The yield was 47 g (65%). The light yellow liquid had b.p. 189-190° (5 mm), $n^{20}D$ 1.6338, d^{20}_4 1.1177.

Found %: C 80.30, 80.19; H 6.78, 6.71; S 12.99, 12.76. $C_{16}H_{16}S$. Calculated %: C 79.95; H 6.71; S 13.34.

TABLE 1

Catalytic Conversions of ar-β -Tetralyl Phenyl Sulfide

Substance	Yield		Boiling point	n_D^{20}	d_4^{20}	Literature data		
	in g	in % catalyzate				boiling point	n_D^{20}	d_4^{20}
Thiophenol	9.7	37.3	60.2—60.5° (14mm)	1.5920	1.0755	71° (15mm)[7]	1.5893 [9]	1.0766 [9]
Tetralin	8.6	33.1	207	1.5505	0.9723	207.4 [10]	1.5415 [11]	0.96935 [11]
Naphthalene	2.0	7.7	M.p. 78.8 *	—	—	M.p. 80.2° [12]	—	—

* Picrate: m.p. 150°. Literature data: 149.5° [13].

TABLE 2

Catalytic Conversions of ac-β -Tetralyl Phenyl Sulfide

Substance	Yield		Boiling point	n_D^{20}	d_4^{20}
	in g	in % catalyzate			
Thiophenol . .	11.6	42.3	65—67° (17mm)	1.5910	1.0757
Tetralin . .	5.5	20.1	60—61 (3mm)	1.5452	0.9668
Naphthalene . .	3.1	11.3	M.p. 80 *	—	—

* See Table 1 for literature data.

Synthesis of ac-β -tetralyl phenyl sulfide. This was carried out by the general method for the preparation of mixed sulfides [6]. In a three-necked flask fitted with a stirrer, dropping funnel, and reflux condenser, 17.4 g of potassium hydroxide was dissolved in 90 ml of alcohol, the solution heated to 70-75°, and 34.1 g of thiophenol added [7]. With the mixture stirred at 80°, 51.6 g of ac-β -chlorotetralin [8] was added dropwise over a period of 0.5 hr and then the reaction mixture was heated at 90° for 3.5 hr. The reaction mixture was cooled, water added to dissolve the potassium chloride, and the sulfide extracted with ether. The ether extract was washed with 10% NaOH solution and water and dried over $CaCl_2$. We obtained 30 g (40.3%) of ac-β -tetralyl phenyl sulfide.

* In the preparation of the diazonium salt it was necessary to avoid excess nitrous acid as this promoted tar formation during the preparation of the sulfide.

B.p. 184.5-185.5° (3 mm), $n^{20}D$ 1.6229. d^{20}_4 1.1263.

Found %: C 79.5, 79.72; H 6.70, 6.75; S 13.92, 13.75. $C_{16}H_{16}S$. Calculated %: C 79.95; H 6.71; S 13.34.

Catalytic conversions of ar- and ac-β-tetralyl phenyl sulfides. A sample (30 g) of sulfide was passed over the aluminosilicate catalyst at 300° under standard conditions [4]. The catalyzate yields were 86.7 and 91% of the starting amounts of sulfides, respectively. The liquid portion of the catalyzate was separated from the solid by filtration and treated first with 10% and then 20% alkali to remove thiophenol. The thiophenol, which was liberated by acidification of the alkaline extracts, was washed with water, dried with Na_2SO_4, and distilled. The alkali-insoluble liquid portion of the catalyzate was washed with water, dried with $CaCl_2$, and distilled. The naphthalene isolated by distillation was combined with the solid portion of the catalyzate and sublimed. The amounts of the substances isolated from the catalyzates, their constants, and literature data are given in Tables 1 and 2.

SUMMARY

1. Previously undescribed ar- and ac-β-tetralyl phenyl sulfides were synthesized.

2. The catalytic conversions of ar and ac-β-tetralyl phenyl sulfides over aluminosilicate catalyst at 300° were studied. It was established that in both cases the bond between the sulfur and the tetralin radical was ruptured. The rupture of this bond in the case of ar-β-tetralyl phenyl sulfide demonstrates that the hexamethylene ring of tetralin weakens the bond of sulfur with the aromatic ring. Rupture of the bond of sulfur with the hexamethylene ring in ac-β-tetralyl phenyl sulfide confirms the relative weakness of the bond of sulfur with an alicycle, which was observed previously.

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THERMAL DECOMPOSITION OF TETRAETHYLLEAD AND HEXAETHYLDIPLUMBANE

II. DECOMPOSITION OF MIXTURES OF TETRAETHYLLEAD, HEXAETHYLDIPLUMBANE AND DIETHYLLEAD

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In a previous communication [1] it was shown that the thermal decomposition of tetraethyllead is a complex chain process, proceeding with the stepwise removal of ethyl radicals through the intermediate formation of less ethylated compounds of lead.

$$(C_2H_5)_4Pb \longrightarrow (C_2H_5)_6Pb_2 \longrightarrow (C_2H_5)_2Pb \longrightarrow Pb \qquad (I)$$

It follows from this that hexaethylplumbane is an intermediate product in the decomposition of tetraethyllead and, in its turn, undergoes decomposition to form diethyllead. This hypothesis was confirmed by a number of experimental facts. Nonetheless, the accumulation of new data supporting the intermediate formation of diethyllead is extremely desirable.

It also seemed interesting to investigate how far the rules observed in the thermal decomposition of tetraethyllead and hexaethyldiplumbane are in accordance with the theory of successive reactions, which has been developed quite fully for simple cases (for example, for the case of a series of successive monomolecular reactions). It seemed to us that this type of comparison could confirm the accuracy of scheme (1) and shed light on the role of the metallic lead formed in the decomposition process.

To solve the problems given above, we studied the thermal decomposition of mixtures of tetraethyllead and hexaethyldiplumbane, on the one hand, and of hexaethyldiplumbane and diethyllead, on the other. In both cases the process was carried out at temperatures that ensured quite rapid decomposition of both components of the mixture.

In addition, it seemed worthwhile to study the processes occurring during the synthesis of hexaethyldiplumbane by Hein and Klein's method [2], as it has been reported that the properties of this substance depend strongly on the preparation conditions.

As a result it was established that the procedure in [2] leads to the formation of mixtures of diethyllead and hexaethyldiplumbane. The composition of the mixtures may be varied by changing the duration of the reaction or by brief heating of the reaction mixture.

PROCEDURE

In preliminary experiments it was observed that the procedure used previously [1], which allowed brief contact between the substances investigated and atmospheric oxygen, did not give reproducible results in the investigation of mixtures of diethyllead and hexaethyldiplumbane. Therefore, this part of the work was carried

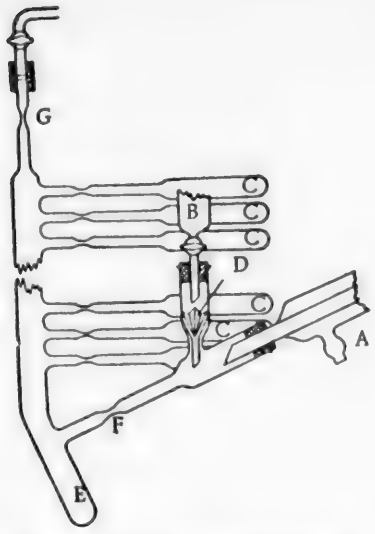

Fig. 1. Receiver of apparatus for tetraethyllead distillation. Explanation in text.

out by a procedure which eliminated contact between the organolead compounds and the atmosphere. Thus, for example, mixtures of tetraethyllead and hexaethyldiplumbane were prepared in an apparatus which consisted of the receiver of an apparatus for vacuum distillation of tetraethyllead in a stream of hydrogen (Fig. 1).

After the normal purification,* the tetraethyllead was placed in a Claisen flask connected to the apparatus through condenser A. Outlet pipe 6 was connected to the vacuum apparatus.

For the introduction of hexaethyldiplumbane, the apparatus was fitted with a separatory funnel B, into which was placed the reaction mixture obtained in the synthesis of hexaethyldiplumbane.

The mixture was prepared in the following way. A calculated amount of tetraethyllead was distilled in a stream of hydrogen at 10 mm residual pressure into section E of the apparatus. At the same time, hexaethyldiplumbane was separated from the aqueous layer of the reaction mixture by means of the separatory funnel B, filtered through the fluted filter D, and mixed with the distilled tetraethyllead. When the mixture had drained into section E, the left-hand part of the apparatus was sealed off from the right-hand part at F. The pressure in the left-hand part of the apparatus was then reduced from 10 to 0.5-1 mm and the apparatus sealed off at G. The mixture was uniformly distributed between the small ampoules C, which were then sealed off at the constrictions. The composition of the mixture obtained was determined spectrophotometrically [3]. The amount of mixture in the ampoules C was established by weighing.

The ampoules C obtained by the method above were kept in a thermostat at 135 ± 0.4° and then frozen in liquid nitrogen. After opening and thawing, the liquid fraction of the ampoules was analyzed spectrophotometrically [3]; the solid fraction (metallic lead) was washed carefully with ether, dissolved in dilute nitric acid, and analyzed by the molybdate method.

A similar procedure was used for studying the thermal decomposition of mixtures of diethyllead and hexaethyldiplumbane.

It has already been mentioned above that in the synthesis of hexaethyldiplumbane by the method of Hein and Klein, even a very slight deviation from the instructions is reflected in the physical and chemical properties of the product. To confirm this, Fig. 2 shows the relation between the optical density of the product and the duration of its synthesis. In all cases the product was obtained by keeping an unstirred mixture of aluminum powder (grain size 0.1-0.4 mm) and a solution of 7 g of triethyllead chloride in 50 ml of 2.5 N KOH in a thermostat at 18 ± 0.2°.

As Fig. 2 shows, the optical density of the product fell regularly with an increase in the time in the thermostat. In parallel, there was a change in the color of the product from bright red (after 2 hr in the thermostat) to yellow with a reddish tinge (9 hr) and an increase in the stability of the substance during storage.

On the basis of these facts it was considered that at the beginning of the synthesis the organic layer formed by the reaction of aluminum with an alkaline solution of triethyllead chloride was not pure hexaethyldiplumbane, but a mixture of it with diethyllead.

During the period in the thermostat (or during heating in the method of Hein and Klein), the organic layer was impoverished in diethyllead by the disproportionation reaction: $3(C_2H_5)_2Pb \rightarrow (C_2H_5)_6Pb_2 + Pb$, due to which there was a decrease in optical density, a change in color, and an increase in the stability of the product during storage.

To demonstrate the accuracy of this hypothesis it seemed worthwhile to study the decomposition kinetics of a series of hexaethyldiplumbane samples obtained with different periods in the thermostat (differing from each

*For the purification of tetraethyllead and the synthesis of hexaethyldiplumbane see [1].

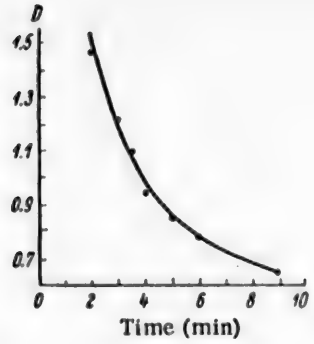

Fig. 2. Change in optical density of hexaethyldiplumbane during its synthesis. Absorption layer thickness d 0.020 mm; wavelength λ 400 mμ.

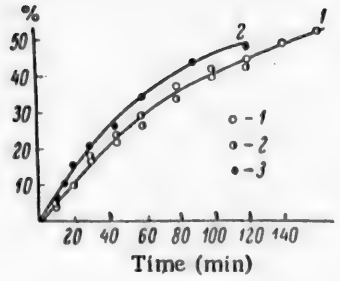

Fig. 3. Kinetic curves of the thermal decomposition of pure tetraethyllead (1), a mixture of 2.3% of hexaethyldiplumbane and 97.7% of tetraethyllead (2), and a mixture of 19.5% of hexaethyldiplumbane and 80.5% of tetraethyllead (3).

other in optical density and other physical properties and, it must be assumed, in the concentration of diethyllead in the hexaethyldiplumbane).

For this purpose, the reaction mixture after being kept in the thermostat was placed in the separatory funnel B of the apparatus illustrated in Fig. 1 with the condenser A replaced by a capillary for the introduction of hydrogen. The organic layer was separated into the apparatus, which was continuously evacuated (0.5-1 mm) and flushed with a stream of purified hydrogen, and filtered through filter D. The subsequent procedure coincided with that described above. The thermal decomposition of the "hexaethyldiplumbane" samples obtained in this way was studied at 85 ± 0.2° (Fig. 5).

DISCUSSION OF RESULTS

Thermal decomposition of mixtures of tetraethyllead and hexaethyldiplumbane. Mixtures containing 2.3, 13.7, and 19.5% of hexaethyldiplumbane were investigated. As previously [1], the process was followed by the rate of formation of the final decomposition product, namely, metallic lead (Fig. 3) and the accumulation of the intermediate decomposition product, hexaethyldiplumbane (Fig. 4).

For comparison, Figs. 3 and 4 give kinetic curves for the thermal decomposition of pure tetraethyllead. From Fig. 3 it follows that the addition of hexaethyldiplumbane slightly accelerates the formation of metallic lead, but the nature of the kinetic curves remains unchanged. Due to this, the kinetic curve for a mixture containing a small amount of additive (2.3%, for example) practically coincided with that for pure tetraethyllead.

It seemed to us that the results obtained agree well with the facts established previously, i.e., since considerable amounts of hexaethyldiplumbane accumulate during the decomposition of tetraethyllead, the introduction of small amounts of this product does not disturb the kinetics of the decomposition.

The accumulation of the intermediate decomposition product is shown as a plot of time against percent content of hexaethyldiplumbane in the tetraethyllead (case A) in Fig. 4. The same process may be expressed graphically in another way, namely, as a plot of time against the number of moles of hexaethyldiplumbane formed (case B).

From Fig. 4 it follows that case A is characterized by the following rules: All the kinetic curves have a maximum and with an increase in the concentration of hexaethyldiplumbane in the starting mixture there is an increase in the absolute size of the maximum, it is displaced toward the ordinate axis, and there is a sharper fall in the descending arms of the curves.

By using the experimental data in Figs. 3 and 4, it is possible to demonstrate that the rules observed are also obeyed in case B.

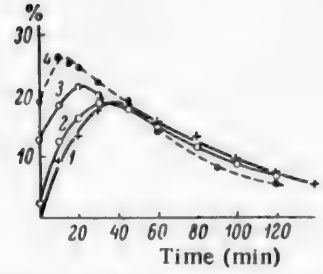

Fig. 4. Change in concentration of hexaethyldiplumbane in tetraethyllead during the thermal decomposition of pure tetraethyllead (1) and a mixture of it with hexaethyldiplumbane. Initial $(C_2H_5)_6Pb_2$ content of mixtures (in weight %): 2.3 (2), 13.7 (3), 19.5 (4).

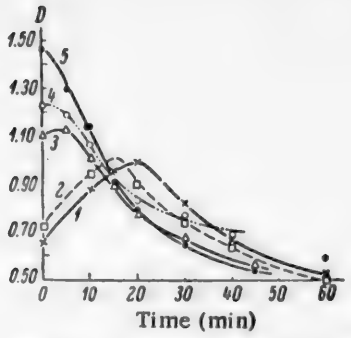

Fig. 5. Curves of change in optical density (d 0.020 mm, λ 400 mμ) during the thermal decomposition of mixtures of hexaethyldiplumbane in diethyllead. The mixtures were prepared by the method of Hein and Klein by keeping the reagents in a thermostat for the following times (in hr): 9 (1), 6 (2), 3.5 (3), 3 (4), 2 (5).

Moreover, it is not difficult to show that the theory of successive conversions is in qualitative agreement with only the rules of case B, but cannot explain the presence of maxima and the descending arms on the kinetic curves in case A.

According to theoretical ideas [4], in the simplest example of two successive monomolecular reactions

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C$$

the accumulation of the intermediate substance B during the decomposition of a mixture of substances A and B is described by the equation:

$$B_t = \frac{k_1 A_0}{k_2 - k_1}\left(e^{-k_1 t} - e^{-k_2 t}\right) + B_0 e^{-k_2 t}, \qquad \text{(II)}$$

where A_0 and B_0 are the numbers of moles of substances A and B in the starting mixture at the moment of time $t = 0$, B_t is the number of moles of intermediate substance at the moment of time t, and k_1 and k_2 are the rate constants of the conversion.

Let us examine the case when $k_2 > k_1$. The curve of the relation between B_t and t has a maximum. By equation the derivative $\frac{dB_t}{dt}$ to zero, we find the time at which the curve passes through the maximum:

$$t_{max} = \frac{\ln k_2 - \ln k_1}{k_2 - k_1} + \frac{1}{k_2 - k_1} \ln\left[1 - \frac{B_0}{A_0}\left(\frac{k_2 - k_1}{k_1}\right)\right]. \qquad \text{(III)}$$

From equation (III) it follows that the time t_{max}, corresponding to the greatest accumulation of substance B in the system, will decrease with an increase in the ratio $\frac{B_0}{A_0}$. The upper limit for t_{max} is the case when $B_0 = 0$.

What has been stated shows that the nature of the curves described by equation (II) is very similar to the nature of the kinetic curves obtained experimentally (case B).

At the same time, the theory of successive reactions does not explain why the kinetic curves illustrated in Fig. 4 (case A) also have maxima and descending arms. These facts may be explained, apparently, by the catalytic action of the metallic lead formed.

Figure 4 shows that in the thermal decomposition of pure tetraethyllead (curve 1), the concentration of hexaethyldiplumbane reached a maximum (≈19%) after 35-40 min; there was then a decrease in concentration. At the same time, if a starting mixture containing 19% of hexaethyldiplumbane was used (curve 4), at the beginning of the decomposition process there was not a decrease, but an increase in the hexaethyldiplumbane concentration. Consequently, the presence of the descending arm of curve 1 may be explained by catalytic decomposition of hexaethyldiplumbane on the metallic lead formed as in the absence of the latter (curve 4)–the intermediate product accumulated.

Decomposition of mixtures of hexaethyldiplumbane and diethyllead. In a previous communication [1] it was shown that diethyllead is an intermediate product in the decomposition of hexaethyldiplumbane. If this is so, then during the combined decomposition of these compounds the rules observed should be largely analogous to those established for the thermal decomposition of mixtures of tetraethyllead and hexaethyldiplumbane with the role of diethyllead in the first case corresponding to that of hexaethyldiplumbane in the second. A comparison of the data presented in Figs. 4 and 5 confirms these ideas.•

Figure 5 shows the change in optical density during the decomposition of a series of mixtures of diethyllead and hexaethyldiplumbane.

In accordance with the rules established previously (Fig. 4), with an increase in the optical density of the starting mixture, i.e., with an increase in the diethyllead concentration, the maximum on the curves is displaced toward the ordinate axis.

From the experimental data in Fig. 4 it also follows that is is possible to choose a starting mixture with a concentration of hexaethyldiplumbane at which the maximum on the kinetic curve is absent or is observed at t = 0. Precisely such concentrations of diethyllead in hexaethyldiplumbane are apparently found with curves 4 and 5 in Fig. 5.

Thus, analogous rules are observed in the decomposition of binary mixtures of tetraethyllead and hexaethyldiplumbane (Fig. 4) and hexaethyldiplumbane and diethyllead (Fig. 5). This is a new argument in favor of the intermediate formation of diethyllead in the decomposition of hexaethyldiplumbane. In addition, this fact shows that the synthesis of Hein and Klein leads to the formation of mixtures of hexaethyldiplumbane and diethyllead. This again confirms the close relationship and ready interconvertibility of ethyl derivatives of lead.

SUMMARY

1. The thermal decomposition of mixtures of tetraethyllead and hexaethyldiplumbane and of hexaethyldiplumbane and diethyllead was studied.

2. New facts are presented in support of the intermediate formation of hexaethyldiplumbane during the decomposition of tetraethyllead and of diethyllead during the decomposition of hexaethyldiplumbane.

3. It is suggested that metallic lead acts as a catalyst in the thermal decomposition of the compounds studied.

4. It was shown that the synthesis of Hein and Klein [2] leads to the formation of mixtures of diethyllead and hexaethyldiplumbane.

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[2] F. Hein and A. Klein, Ber. 71, 2381 (1938).

[3] N. K. Rudnevskii and N. N. Vyshinskii, Izvest. Akad. Nauk SSSR, Ser. Fiz. 23, 1228 (1959).

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• This comparison is admissible as the optical density in the given case may be considered as proportional to the diethyllead concentration.

••Original Russian pagination. See English translation.

SYNTHESIS AND POLYMERIZATION OF N-ACYLAMIDES OF ACRYLIC ACIDS

O. M. Sleptsova and M. M. Koton

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N-Acylamides of unsaturated acids have been unknown up to now; the acetylation of acrylamide, methacrylamide, and a number of amides of unsaturated acids with ketene was described only recently [1]. At the same time, N-acylamides of saturated acids are well known [2] and are obtained by various methods. The commonest method of preparing N-acylamides of saturated acids is the reaction of amides (acetamide and propionamide) with acid anhydrides (acetic or propionic) in the presence of various catalysts (H_2SO_4, HCl, and CH_3COCl) [3, 4]. In most cases the N-acylamides are obtained in low yields due to side reactions and the difficulty of separating the N-acylamides from the starting amides. In order to study the polymerization capacity of N-acylamides of acrylic acids we synthesized N-acetylmethacrylamide and N-acetyl-α-fluoroacrylamide by the reaction with acetic anhydride in the presence of acetyl chloride as a catalyst according to the equation:

$$CH_2=C(R)CONH_2+(CH_3CO)_2O\rightarrow CH_2=C(R)CONHCOCH_3+CH_3COOH,$$

where R = CH_3 or F.

N-Acetylmethacrylamide was obtained as a colorless liquid with b.p. 82° (2 mm) and N-acetyl-α-fluoroacrylamide as a white crystalline substance with m.p. 70°.

The N-acylamides of acrylic acids we obtained could be used as the starting materials for preparing various polymers and copolymers. N-Acetylmethacrylamide and N-acetyl-α-fluoroacrylamide polymerized readily in the presence of initiators of the radical type to form soluble, thermoplastic masses.

EXPERIMENTAL

Synthesis of N-acetylmethacrylamide. Into a flask with a reflux condenser were placed 17 g of methacrylamide, 21 g of acetic anhydride, and 1 ml of acetyl chloride and 0.05 g of pyrogallol and 0.5 g of copper turnings were added to prevent polymerization. The mixture was boiled for 0.5 hr with a bath temperature of 142-145° and was then vacuum distilled on a Vigreux column. The volatile products (acetonitrile and acetic acid) distilled first and then 12 g (47%) of the main fraction with b.p. 80-82° (2 mm). The product was purified to remove acetamide and methacrylic acid. The amide was separated by freezing twice at 0-3°, the precipitated crystals removed by filtration, and the filtrate distilled twice for separation from methacrylic acid. The pure N-acetylmethacrylamide was a colorless sirupy liquid with a very weak smell. It was soluble in water, alcohol, ether, benzene, acetone, and methyl methacrylate and insoluble in ligroin.

B.p. 82° (2 mm), d^{20}_4 1.0819, $n^{20}D$ 1.4830, MR_D 33.57; calc. 33.06.

Found %: N 11.04; bromine number 126.3. M 128.1. $C_6H_9O_2N$. Calculated %: N 11.01; bromine number 125.7. M 127.1.

Determination of active hydrogen by the Chugaev-Tserevitinov method. Number of H atoms found: 1.02, 1.07. $C_6H_9O_2N$. Number of H atoms calculated: 1.

Our data from the synthesis of N-acetylmethacrylamide do not agree with the data of American authors [1], who identified the substance they obtained as N-acetylmethacrylamide by the nitrogen analysis only. In the "melting point" column, these authors reported "decomposes at 300°" while according to our data N-acetylmethacrylamide is a liquid at normal temperatures.

Synthesis of N-acetyl-α-fluoroacrylamide. This was analogous to the synthesis of N-acetylmethacrylamide, with the difference that when the volatile reaction products had been distilled, the solid residue was recrystallized from ligroin (80-100°); the yield was 33%. For final purification to remove amide, the product was recrystallized three more times.

Pure N-acetyl-α-fluoroacrylamide was a white, crystalline substance, which dissolved in water, alcohol, ether, benzene, and methyl methacrylate. It had m.p. 70°.

Found %: C 45.80; H 4.88; N 10.18; F 14.40. M 131.8. $C_5H_6O_2NF$. Calculated %: C 45.80; H 4.57; N 10.68; F 14.48. M 131.1.

Polymerization of monomers. N-Acetylmethacrylamide was polymerized in glass ampoules, which were evacuated after filling and sealed off at a residual pressure of 1 mm. Benzoyl peroxide (0.12%) and azoisobutyrodinitrile (0.12%) were used as initiators. The ampoules were heated at 50° for 2 hr and then at 40° until the polymer came loose from the glass of the ampoule, after which the temperature was gradually raised in steps up to 120°, being held for 2 hr at each 20° interval and then for 4 hr at 120°, and finally the ampoules were gradually cooled.

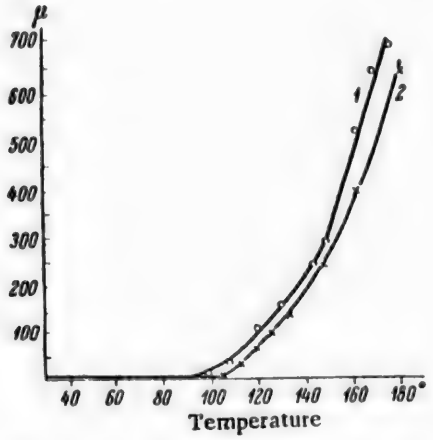

Fig. 1. Temperature-deformation curves for poly-N-acetylmethacrylamide. Explanation in text.

Determination of residual monomer in the polymer. For determination of the residual monomer in a block polymer, 0.5 g of vitreous polymer was dissolved in 50 ml of glacial acetic acid (with heating in a flask with a reflux condenser); then 100 ml of water was added to the solution, and the precipitated polymer removed by filtration and washed with water. The filtrate and wash waters were collected in one flask, their total volume adjusted to 250 ml with water, 50 ml of 0.02 N bromide-bromate solution and 10 ml of hydrochloric acid (d 1.19) added, and the solution left for 20 min in the dark. Then 10 ml of 20% KI solution was added and the liberated iodine titrated with 0.01 N hyposulfite solution in the presence of starch. The amount of monomer was calculated from the following formula

$$\text{Amount of monomer (in \%)} = \frac{(a-b) \cdot 0.000635 \cdot 100}{c},$$

where a is the number of milliliters of 0.01 N hyposulfite solution consumed in a blank experiment, b is the number of milliliters of 0.01 N hyposulfite solution consumed in titrating the sample and c is the weight of the polymer sample (in g).

The results of determining the residual monomer (in %) in poly-N-acetylmethacrylamide polymerized in the presence of different initiators were as follows: benzoyl peroxide 1.83, 1.09; azoisobutyrodinitrile 3.75, 3.94.

The block polymer of N-acetylmethacrylamide was a transparent, colorless glass that did not change in transparency or acquire a color during prolonged (more than 8 months) storage under room conditions. The specific gravity at 20° was 1.260. It was soluble in glacial acetic acid and insoluble in water and benzene.

For determining the properties of a polymer which had been freed from monomer and low-molecular fractions, powdered polymer was extracted with methanol for 20 hr in a Soxhlet apparatus.

Analysis of extracted polymer:

Found %: N 11.28. $(C_6H_9O_2N)_n$. Calculated %: N 11.01.

The characteristic viscosity of the polymer determined in dimethylformamide solution at 20° was 3.0.

For determination of the vitrification temperature and the temperature dependence of deformation, polymer powder was pressed into tablets 3 mm thick and 8 mm in diameter at 190° and a pressure of 480 kg/cm². Figure 1 shows thermomechanical curves for block (1) and extracted (2) poly-N-acetylmethacrylamide. The vitrification temperature for 1 was 90° and for 2, 102°.

N-Acetyl-α-fluoroacrylamide polymerized readily on fusion without an initiator.

Polymerization of N-acetyl-α-fluoroacrylamide in aqueous solution. A sample (1.00 g) of N-acetyl-α-fluoroacrylamide was dissolved in 9.5 ml of water and 0.5 ml of 1% hydrogen peroxide solution added. The solution was heated at 60° for 0.5 hr with stirring and then cooled. The curdy white polymer which precipitated was collected on a Schott funnel, washed with cold distilled water, and dried to constant weight in a vacuum desiccator. We obtained 0.67 g (67%) of polymer. The polymer was pressed into tablets weighing 0.3 g at 160° and a pressure of 480 kg/cm². The tablets were transparent, slightly brown glasses. The thermomechanical curve for poly-N-acetyl-α-fluoroacrylamide is given in Fig. 2. The vitrification temperature was 150°.

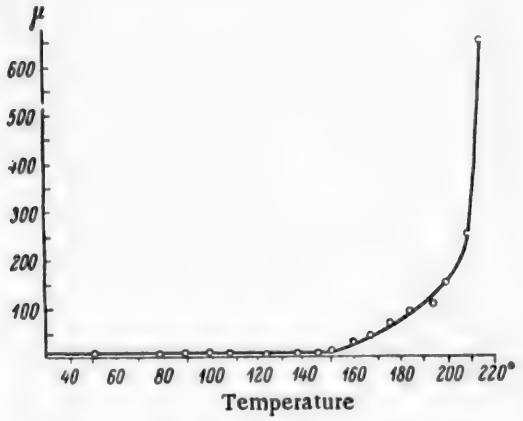

Fig. 2. Temperature-deformation curve for poly-N-acetyl-α-fluoroacrylamide.

Polymerization in ethyl acetate. A sample (0.77 g) of N-acetyl-α-fluoroacrylamide and 0.005 g of benzoyl peroxide were dissolved in 8 ml of ethyl acetate. The solution was heated gradually to 75° over a period of 2 hr with stirring and kept at this temperature for 15 min. We obtained 0.31 g (40%) of polymer. The vitrification temperature of the polymer was 128°. The viscosity determined in dimethylformamide at 20° was 0.6. The poly-N-acetyl-α-fluoroacrylamide was soluble in water, dimethylformamide, and ethyl acetate.

SUMMARY

1. N-Acetylmethacrylamide and N-acetyl-α-fluoroacrylamide, which have not been described in the literature previously, were synthesized and characterized.

2. It was established that N-acetylmethacrylamide undergoes block polymerization under the action of benzoyl peroxide and azoisobutyrodinitrile. N-Acetyl-α-fluoroacrylamide polymerizes in solution under the action of hydrogen peroxide and benzoyl peroxide. Some properties of the polymers were investigated.

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FURAN COMPOUNDS

XII. NEW DATA ON THE ELECTROLYTIC METHOXYLATION OF FURAN COMPOUNDS

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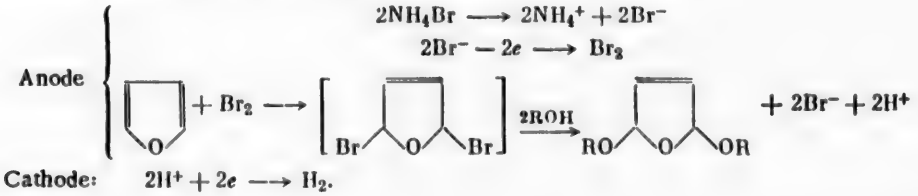
In the first experiments on the alkoxylation of furan compounds, solutions of the latter in the appropriate alcohol were treated with bromine with cooling [1]. This method was used to prepare many 2,5-dialkoxy-2,5-dihydrofurans and their properties and conversions were studied [2].

In 1952 Clauson-Kaas and his co-workers [3] developed a more convenient method of alkoxylation by electrolysis of a solution of the furan compounds in the appropriate alcohol at low temperature (from -14 to -20°). A small amount of ammonium bromide was introduced into the solution as the electrolyte; other mineral and organic salts (NH_4NO_3, $NaNO_3$, and HCOONa) and also H_2SO_4 and BF_3 etherate could be used for these purposes, but the yields were reduced in this case [4].

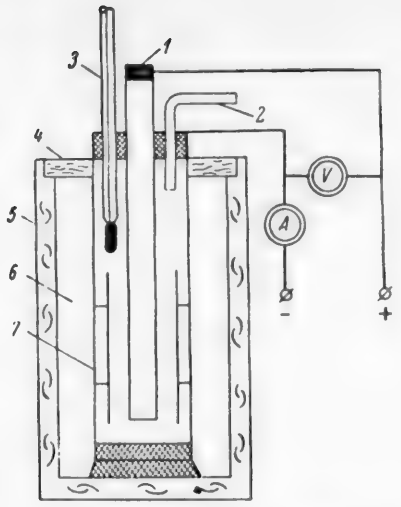
The electrolyzer consisted of a cathode which was formed by two nickel-coated brass cylinders, one inside the other, and an anode formed by a porcelain tube covered with platinum foil. An electrolyzer for small amounts of materials was proposed later [5].

The reaction mechanism has not been studied adequately. Clauson-Kaas, Limborg, and Glens [3] considered that an oxidative process occurs. The bromine liberated at the anode reacts with the furan in the 1,4 position to form the dibromo derivative, which reacts which alcohol to give the dialkoxydihydrofuran and HBr; the latter combines with ammonia liberated at the anode to regenerate ammonium bromide.



By using this method, Clauson-Kaas and other authors [3, 6-8] were able to synthesize in yields of 60-90% the corresponding dihydroxydihydrofuran compounds from furan, sylvan, furfuryl alcohol and its acetate and methyl ether, methyl pyromucate, 3-isopropylfuran, 4-isopropylfurfural dimethyl acetal, a number of furfurylamine derivatives, methylfurylcarbinol, etc.; some of these were then used for the preparation of derivatives of pyrrole, pyridine, pyridazine, etc.

Our experiments on electrolytic alkoxylation were largely concerned with furan compounds containing an ester group or a carbonyl in position 3 or 4 in the side chain.



Plan of electrolyzer for alkoxylation. 1) Carbon anode; 2) gas outlet tube; 3) thermometer; 4) lid of vessel; 5) vessel for cooling mixture; 6) cooling mixture; 7) nickel cathode.

We largely kept to the procedure proposed by Clauson-Kaas and used ammonium bromide as the electrolyte. However, we introduced substantial changes into the construction of the electrolyzer, which consisted primarily of replacing the platinum electrode by a carbon one, making the apparatus itself and the method more accessible both under laboratory and under production conditions. Sheet nickel was used as the material for the cathode. The plan of the electrolyzer is given in the figure.

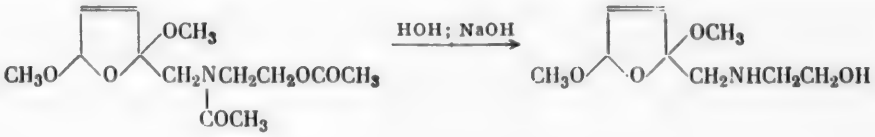
A bank of batteries or a VSA-5 rectifier was used as a current source. The amount of electricity passed through the solution was determined with a copper coulometer.

For cooling we used butyl alcohol to which solid carbon dioxide was added until the required temperature was reached in the electrolyzer.

The new electrolyzer was first tested on the methoxylation of furan, sylvan, and furfuryl acetate, which had been studied previously by Clauson-Kaas. A comparison of our results with the data of the above authors shows that the yields of the corresponding dimethoxydihydrofuran compounds when our electrolyzer was used were in general not lower and, in some cases, even higher than in an electrolyzer with a platinum anode (Table 1).

Then, in the same electrolyzer we methoxylated the acetates of 1-(α-furyl)-propanol-3 and 1-(α-furyl)-butanol-3, 1-(α-furyl)-butanone-3, the acetate of N-acetylfurfurylaminoethanol, and also 1-(α-furyl)-3-methylpentane [10]. In all cases we obtained quite satisfactory yields of the corresponding dimethoxydihydrofuran compounds.

We were unable to isolate the dimethoxydihydrofuran derivative from the acetate of N-acetofurfurylaminoethanol as such; the reaction product was hydrolyzed with alkali without purification according to the scheme:

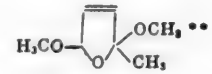
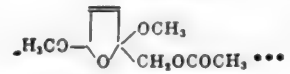
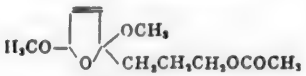
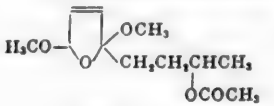
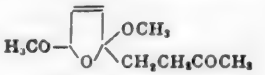
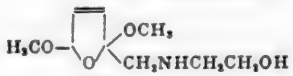
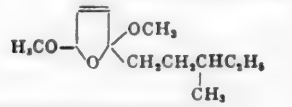


Data on the properties of all the dimethoxydihydrofurans obtained in this way and also the analyses are given in Table 2.

TABLE 1

Starting compound	Yield of dimethoxydihydrofuran compound			
	electrolyzer with platinum anode [3, 6]		electrolyzer with carbon anode	
	in % on current	on amount of starting material (in %)	in % on current	on amount of starting material (in %)
Furan	86	73	92	78
Sylvan	81	69	85.1	71.4
Furfuryl acetate	86	87	81.5	83.3

TABLE 2

Formula	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Molecular weight found	Molecular weight calculated	MR_D found	MR_D calculated	% C found	% C calculated	% H found	% H calculated	% N found	% N calculated
•	78	158—160° (760)	—	1.4326 (at 25°)	—	—	—	—	—	—	—	—	—	—
 ••	67	158—160 (760)	—	1.4289	—	—	—	—	—	—	—	—	—	—
 •••	68.5	118—120 (12)	—	1.4458	—	—	—	—	—	—	—	—	—	—
	46 7	105—105.5 (1)	1.105	1.4578	248.6	230.25	56.59	56.23	57.12, 57.26	57.38	8.32, 7.74	7.88	—	—
	67.1	133—134 (7)	1.0743	1.4526	238.3	244.28	61.42	61.53	59.15, 59.44	59.00	8.27, 8.36	8.25	—	—
	51.5	103—104 (2)	1.077	1.4568	202.5	200.2	50.64	50.65	60.42, 60.59	59.98	8.39, 8.46	8.06	—	—
	55.0	120—122 (1.5)	1.134	1.4750	213	203.2	50.46	51.15	53.19	53.19	8.98	8.43	7.34, 7.21	6.89
	51	99—101.5 (5)	0.9676	1.4461	—	—	59.07	59.88	66.92	67.26	10.61	10.35	—	—

•Literature data [3]: b.p. 160-162° (760 mm), $n^{25}D$ 1.4329.

••Literature data [6]: b.p. 158-159° (760 mm), $n^{25}D$ 1.4265.

•••Literature data [6]: b.p. 119° (12 mm), $n^{25}D$ 1.4433.

TABLE 3

Formula	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Molecular weight		MR_D		% C		% H		% N	
					found	calculated	found	calculated	found	calculated	found	calculated	found	calculated
	84.4	142—143° (6)	1.0472	1.4420	258	246.3	62.23	62.099	58.61, 58.85	58.51	9.15, 9.06	9.00	—	—
	67.5	124.5—126.5 (4)	1.040	1.4432	210.2	202.2	51.58	51.12	59.50, 59.18	59.39	9.45, 9.60	8.97	—	—
	86.6	124.5—125 (1.5)	1.115	1.4630	208	205.2	51.13	51.62	52.77, 52.68	52.67	9.22, 8.82	9.33	6.92, 6.96	6.83

Many of the dimethoxydihydrofuran compounds we obtained were then converted into the corresponding dimethoxytetrahydrofuran compounds by hydrogenation in alcohol solution under pressure at 20-40° in the presence of Raney nickel. The reaction proceeded rapidly and gave good yields. Data on the properties of the dimethoxytetrahydrofuran compounds and the analyses are given in Table 3.

EXPERIMENTAL •

The furan compounds were methoxylated by a standard procedure, of which typical examples are given below.

Preparation of the acetate of 2,5-dimethoxy-2,5-dihydrofurylbutanol-3. A mixture of 49.9 g of the freshly distilled acetate of 1-(α-furyl)-butanol-3 and 5 g of ammonium bromide was dissolved in 250 ml of methanol. The solution obtained was poured into the electrolyzer, cooled to -12°, and electrolyzed for 10 hr with a current of 3.5-1.8 a passed through the electrolyzer at 6-30 v. After the electrolysis, the solution was transferred to a flask and sodium methylate (1.2 g of metallic sodium in 20 ml of methanol) added to it. The methanol and ammonia were removed on a water bath under reduced pressure; the sodium bromide precipitate which formed was removed by filtration and washed several times with ether. The residue after removal of the ether was vacuum distilled to give a fraction with b.p. 133-134° (7 mm). Analysis data of the acetate of dimethoxydihydrofurylbutanol-3 obtained are given in Table 2.

The acetate of 1-(α-furyl)-propanol-3, 1-(α-furyl)-butanone-3, 1-(α-furyl)-3-methylpentane [10], furan, sylvan, and furfuryl acetate were methoxylated analogously. Data on the methoxylation conditions for these compounds are given in Table 4.

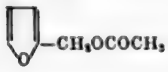
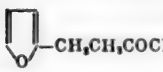
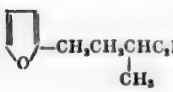
The properties and analyses of the dimethoxydihydrofuran compounds obtained are presented in Table 2.

2,5-Dimethoxy-2,5-dihydrofurfurylaminoethanol. A mixture of 50 g of the freshly distilled acetate of N-acetofurfurylaminoethanol•• and 5 g of ammonium bromide was dissolved in 230 ml of methanol. The solution obtained was poured into the electrolyzer, cooled to -14°, and electrolyzed for 8 hr with a current of 3.5-2.3 a at 6-11 v. After the electrolysis, the slightly yellowish

•I. S. Monakhova assisted with a number of experiments.

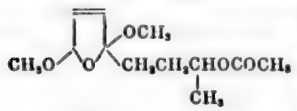
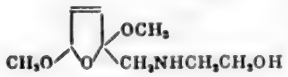
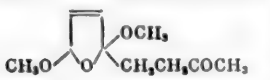
••See [9] for the preparation. According to more accurate data, the boiling point of furfurylideneaminoethanol is 124° (6 mm), furfurylaminoethanol 99-100° (2 mm), and the acetate of N-acetofurfurylaminoethanol 152-153° (2 mm) and the latter has $n^{20}D$ 1.4918 and d^{20}_4 1.158.

TABLE 4

Formula	Amt. of starting material (moles)	Current strength (in a)	Voltage (in v)	Temperature in cell	No. of ampere-hour
	0.5	3.9—3.0	—	—12°	22.7
	0.5	3.5—2.8	6—12	—16	22.5
	0.3	3.0—2.9	8—13	—13	21.0
	0.3	3.7—2.5	5—15	—14	23.0
	0.39	3.5—3.0	5—14	—13	26.0
	0.09	3.0—1.5	9—11	—14	8.9

Note: In all experiments 230-250 ml of methanol was used. The electrolyte was NH_4Br.

TABLE 5

Formula	Amt. of substance (moles)	Temperature	Pressure (in atm)
	0.08	30°	100—120
	0.098	40	60—100
	0.1	20	50—75

Note: The catalyst was Raney nickel (1.5 g). The solvent was CH_3OH (20 ml).

liquid was transferred from the electrolyzer to a flask and sodium methylate (1.2 g of sodium in 20 ml of methanol) added. The methanol and ammonia were removed by distillation and 250 ml of 3 N NaOH solution was added to the residue. The mixture was heated for 20 hr in a 0.5-liter Kjeldahl flask with a reflux condenser. The solution was then extracted with chloroform (three 50-ml portions) and the extract dried over baked potassium carbonate. The chloroform was removed under reduced pressure on a water bath and the residue vacuum distilled at 1.5 mm to yield a fraction with b.p. 120-122° (see Table 2).

Hydrogenation of dimethoxydihydrofuran compounds. The hydrogenation was carried out in a rotating steel autoclave with a capacity of 150 ml; a set furnace temperature was maintained by means of an MRShchPr-54 electronic thermoregulator.

Data on the conditions for the hydrogenation of the acetate of dimethoxydihydrofurylbutanol-3, dimethoxydihydrofurfurylaminoethanol, and dimethoxydihydrofurylbutanone-3 is given in Table 5.

Data on the physical properties and analyses of the dimethoxytetrahydrofuran compounds obtained as a result of the hydrogenation are given in Table 3.

SUMMARY

1. An electrolyzer of a new design with a carbon anode and a nickel cathode is proposed for the alkoxylation of furan compounds. It was shown that it is as efficient as an analogous apparatus with a platinum anode.

2. The acetates of 1-(α-furyl)-propanol-3 and 1-(α-furyl)-butanol-3, 1-(α-furyl)-butanone-3, the acetate of N-acetofurfurylaminoethanol, and 1-(α-furyl)-3-methylpentane were methoxylated and the properties of the five new 2,5-dimethoxydihydrofuran compounds thus obtained are described.

3. A description is also given of the properties of the previously unknown 2,5-dimethoxytetrahydrofuryl butanone-3, the acetate of 2,5-dimethoxytetrahydrofurylbutanol-3, and 2,5-dimethoxytetrahydrofurfurylaminoethanol, which were obtained by hydrogenation of the corresponding dimethoxydihydrofuran compounds.

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FORMATION OF COMPLEXES OF AMINES WITH VARIOUS ORGANIC COMPOUNDS

I. COMPLEXES OF BENZIDINE AND NAPHTHYLAMINES WITH SOME HALOPHENOLS

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A large number of complex compounds of amines with phenols have been described in the literature. These complexes are formed due to the formation of a bond (hydrogen) between the hydrogen of the phenol hydroxyl group and the nitrogen of the amine. Complex compounds have not been isolated from many systems of this type, but reaction between the components has been observed by various physicochemical analysis methods. A number of examples were given in our previous communication [1].

In the present work we studied the formation of complexes of benzidine, α-naphthylamine, and β-naphthylamine with some halogen derivatives of phenols. The complexes were almost always obtained by mixing solutions of the components in a suitable solvent, most frequently benzene; sometimes they were again recrystallized and then analyzed for nitrogen (by the Kjeldahl method) and in some cases, for halogen. The experimental results are given in Table 1.

TABLE 1

Sample No.	Amines	Phenols	Mol composition of complexes	Melting point
1	Benzidine . . .	4-ClC_6H_4OH	1 : 2	122—123°
2	Benzidine . . .	4-BrC_6H_4OH	1 : 2	123—124
3	Benzidine . . .	4-IC_6H_4OH	1 : 2	149—150
4	α-$C_{10}H_7NH_2$ . .	4-ClC_6H_4OH	1 : 1	40—41
5	α-$C_{10}H_7NH_2$ . .	4-BrC_6H_4OH	1 : 1	52—53.5
6	α-$C_{10}H_7NH_2$ . .	4-IC_6H_4OH	1 : 1	61—62
7	β-$C_{10}H_7NH_2$ . .	4-ClC_6H_4OH	1 : 1	70—71
8	β-$C_{10}H_7NH_2$ . .	4-BrC_6H_4OH	1 : 1	71—73
9	β-$C_{10}H_7NH_2$ . .	4-IC_6H_4OH	1 : 1	88—89

The compounds synthesized were tested for bactericidal activity. Some of them gave a positive result and on some examples it was shown that the action of the complex was different from that of the amine and phenol separately. The bactericidal action was determined by the suspension method with a culture of B. coli in a meat infusion broth. The phenol resistance of the strain was 20 min in a 1 : 90 solution of phenol. The effective concentration and the treatment time were established rather than the phenol coefficient [6, 7]. The experimental results are given in Table 2.

TABLE 2

Bactericidal Action of Complex Compounds and Their Components on B. coli

Sample No.	Substances tested	Conc. of substance (in %)	Bactericidal action with the following exposure (in min)	
			20	40
1	Benzidine + 4-chlorophenol	0.5	−	+
2	Benzidine + 4-bromophenol	0.295	−	+
3	Benzidine + 4-iodophenol	0.248	−	−
4	α-Naphthylamine + 4-chlorophenol	0.483	+	+
5	α-Naphthylamine + 4-bromophenol	0.314	+	+
6	α-Naphthylamine + 4-iodophenol	0.414	±	+
7	β-Naphthylamine + 4-chlorophenol	0.258	−	+
8	β-Naphthylamine + 4-bromophenol	0.283	±	+
9	β-Naphthylamine + 4-iodophenol	0.411	±	+
	Benzidine	0.43	−	−
	α-Naphthylamine	0.5	±	+
	β-Naphthylamine	0.493	−	−
	4-Chlorophenol	0.518	+	+
	4-Bromophenol	0.513	−	+
	4-Iodophenol	0.284	±	+

Note: Plus (+) denotes the absence of growth of the test organism (i.e., the presence of bactericidal action); minus (-) denotes the presence of growth of the test organism; plus-minus (±) denotes the presence of growth of B. coli in one test and the absence of growth in another.

EXPERIMENTAL

Preparation of starting materials. The amines used were normal reagents which were purified by recrystallization. The 4-chlorophenol was prepared [2] by chlorination of phenol with dichlorourea. 4-Bromophenol was prepared by bromination of phenol with dioxane dibromide [3] and also by bromination with dichlorourea and potassium bromide [4]. 4-Iodophenol was synthesized from p-aminophenol in the presence of potassium iodide and copper bronze [5].

Synthesis of Complexes

1. Benzidine-4-chlorophenol complex. To 1.84 g of benzidine in 50 ml of benzene was added a hot solution of 1.28 g of 4-chlorophenol in 5 ml of benzene. The precipitate consisted of lustrous gray crystals. The same substance was obtained by mixing equimolecular amounts of the starting components.

Found %: N 8.48. $C_{18}H_{17}ON_2Cl$. Calculated %: N 8.95.

The crystals were readily soluble in methyl and ethyl alcohols and insoluble in water, chloroform, and carbon tetrachloride.

2. Benzidine-4-bromophenol complex. This complex was prepared from saturated benzene solutions of the starting materials. Recrystallization from benzene yielded white platelets.

Found %: N 5.66, 5.43. $C_{24}H_{22}O_2N_2Br_2$. Calculated %: N 5.28.

The substance was readily soluble in methyl and ethyl alcohols, ether, and acetone and difficultly soluble in water and chloroform.

3. Benzidine-4-iodophenol complex.* To a hot solution of 0.72 g of benzidine in 25 ml of benzene was added a solution of 1.74 g of iodophenol in 10 ml of benzene. The precipitate of white lustrous platelets was recrystallized from the same solvent.

*M. A. Kuchmar assisted with experiments 7 and 9.

Found %: N 4.73, 4.70. $C_{24}H_{22}O_2N_2I_2$. Calculated %: N 4.44.

The complex was soluble in water (with heating), alcohol, benzene, and chloroform and difficultly soluble in hydrochloric acid and alkali.

4. α-Naphthylamine-4-chlorophenol complex. To a saturated solution of α-naphthylamine containing 1.43 g of substance was added a hot solution of 1.3 g of 4-chlorophenol in 1.5 ml of benzene. The precipitate, which formed rapidly, was recrystallized.

Found %: N 5.64; Cl 12.83. $C_{16}H_{14}ONCl$. Calculated %: N 5.16; Cl 13.0.

The crystals were soluble in alcohol, ether, chloroform, xylene, and acetone and difficultly soluble in cold water.

5. α-Naphthylamine-4-bromophenol complex. The compound was obtained by mixing hot, saturated benzene solutions, containing 0.01 mole each of the starting substances. Violet crystals precipitated after 1 hr.

Found %: N 4.66. $C_{16}H_{14}ONBr$. Calculated %: N 4.43.

The complex was soluble in benzene, alcohol, ether, acetone, chloroform, and ligroin and insoluble in water.

6. α-Naphthylamine-4-iodophenol complex. To 0.71 g of α-naphthylamine in 50 ml of hot ligroin was added a hot, saturated solution containing 1.10 g of 4-iodophenol. Needlelike crystals precipitated after 0.5 hr.

Found %: N 4.12, 3.98. $C_{16}H_{14}ONI$. Calculated %: N 3.83.

The compound was soluble in methyl and ethyl alcohols and in hot ligroin.

7. β-Naphthylamine-4-chlorophenol complex. A molecular ratio of components of 1 : 1 in a saturated benzene solution gave a precipitate, which formed white lustrous crystals on recrystallization.

Found %: N 5.36; Cl 12.01. $C_{16}H_{14}ONCl$. Calculated %: N 5.16; Cl 13.0.

The substance was readily soluble in alcohol, acetone, chloroform, and xylene, difficultly soluble in ether, and very difficultly soluble in cold water.

8. β-Naphthylamine-4-bromophenol complex. The compound was obtained by mixing hot, saturated benzene solutions of the components. It formed white crystals.

Found %: N 4.49, 4.66. $C_{16}H_{14}ONBr$. Calculated %: N 4.43.

9. β-Naphthylamine-4-iodophenol complex. To 1.13 g of β-naphthylamine in ligroin was added a hot ligroin solution of 1.74 g of 4-iodophenol. The crystals obtained had a pink tinge. The same complex was formed if benzene or water was used as the solvent and also when equimolecular amounts of the starting materials were mixed.

Found %: N 4.04, 4.16. $C_{16}H_{14}ONI$. Calculated %: N 3.83.

The crystals were readily soluble in chloroform and with heating in ligroin, benzene, water, and alcohol; they were difficultly soluble in alkali and hydrochloric acid.

SUMMARY

Nine complex compounds of amines with halophenols, which have not been described in the literature, were prepared. The complexes synthesized were tested for bactericidal action.

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SYNTHESIS OF SULFUR COMPOUNDS OF NAPHTHALENES AND THEIR CONVERSIONS ON AN ALUMINOSILICATE CATALYST

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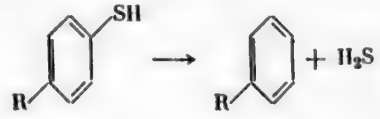
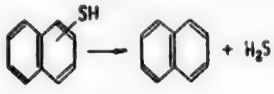
In studying the conversions of sulfur compounds of naphthalenes on an aluminosilicate catalyst, we aimed at determining whether these conversions were analogous to those of sulfur compounds of benzenes, which we had already studied, and whether there was a difference in the behavior of isomeric α- and β-sulfur derivatives of naphthalene on aluminosilicate at 300°.

As we have shown previously [1, 2], the main direction of the conversions of aromatic thiols on an aluminosilicate catalyst is their conversion to the corresponding aromatic hydrocarbons and hydrogen sulfide.



(1)

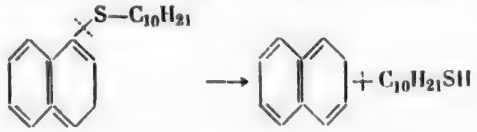
A study of the contact conversions of α- and β-thionaphthols showed that when passed over aluminosilicate under the conditions we adopted [3] they were converted to naphthalene and hydrogen sulfide. The amount of naphthalene isolated in the case of α-thionaphthol was 51.6% of the weight of the catalyzate and in the case of β-thionaphthol, 41.5%.



(2)

Experiments showed that isomeric α- and β-thionaphthols behaved identically both qualitatively and quantitatively. A comparison of schemes 1 and 2 shows that the conversions of thionaphthols are the same as those of thiols of the benzene series.

As we established previously [1], when mixed sulfides are passed over aluminosilicate at 300°, the sulfide molecule is cleaved at one of the bonds of sulfur with a radical and the position of cleavage is determined by the nature of the radicals. It was found that the strongest bond in mixed sulfides is the bond between a benzene ring and sulfur, the weakest bond is that between naphthene rings and sulfur, and the bond between an alkyl and sulfur occupies an intermediate position. In the light of this data we studied the behavior of mixed α- and β-sulfides of naphthalenes on aluminosilicate at 300°. As a result of contact with this catalyst [3], α-naphthyl decyl sulfide was converted into naphthalene (36% of the catalyzate weight), decyl mercaptan (13.1%), decene (7.8%), and hydrogen sulfide. The decomposition scheme for this sulfide is as follows:



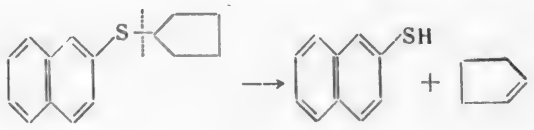
(3)

The primary reaction is rupture of the bond between the sulfur and the naphthalene nucleus with the formation of naphthalene and decyl mercaptan. The secondary process is the elimination of hydrogen sulfide from decyl mercaptan with the formation of decene. This reaction has been observed previously [3].

In contact with aluminosilicate under the same conditions, another sulfide of the α-naphthalene series, α-naphthyl cyclopentyl sulfide gave naphthalene (40.0% of the catalyzate weight), cyclopentanethiol (6.6%), dicyclopentyl sulfide (2.2%), and hydrogen sulfide. The decomposition of this sulfide proceeds according to a scheme analogous to scheme 3. As in the previous case, the primary process is rupture of the bond between the sulfur and the naphthalene nucleus with the formation of naphthalene, and the secondary process is the formation of dicyclopentylsulfide from two molecules of cyclopentanethiol with the liberation of hydrogen sulfide. We have previously observed the formation of a sulfide from the corresponding mercaptan on contact with aluminosilicate [3].

On comparing the behavior of mixed sulfides of the benzene series with that of mixed sulfides of the α-naphthalene series under the same conditions on an aluminosilicate catalyst (scheme 3), one notices a considerable difference in the strength of the bonds of sulfur with the radicals. With mixed sulfides of the benzene series the bond between the sulfur and the benzene ring is strong and the bond between the sulfur and the other radical is broken, while the bond between the naphthalene ring and the sulfur was broken with mixed sulfides of the α-naphthalene series. This bond was found to be the weakest and was even weaker than the bond between sulfur and a naphthene ring, which we had regarded as the most vulnerable until now.

Passing mixed sulfides of the β-naphthalene series over an aluminosilicate catalyst gave quite different results. When passed over aluminosilicate, β-naphthyl cyclopentyl sulfide gave β-thionaphthol (15.6% of the catalyzate weight), cyclopentene (10.2%), naphthalene (43.5%), and hydrogen sulfide. The decomposition scheme for this sulfide is as follows:

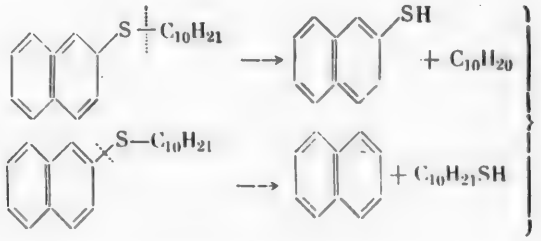


(4)

The primary process is rupture of the bond between sulfur and the cyclopentyl radical with the formation of β-thionaphthol and cyclopentene, and the secondary process is conversion of the β-thionaphthol formed into naphthalene and hydrogen sulfide.

Consequently, in the case of β-naphthyl cyclopentyl sulfide (scheme 4), decomposition of the molecule proceeds analogously to decomposition of mixed sulfides of the benzene series and contrary to decomposition of mixed sulfides of the α-naphthalene series.

When passed over aluminosilicate under the same conditions, another sulfide of the β-naphthalene series, β-naphthyl decyl sulfide, gave β-thionaphthol (1.1% of the catalyzate weight), decyl mercaptan (6%), naphthalene (30.5%), decene-decane fraction (4.2%), and hydrogen sulfide. In this case decomposition of the sulfide molecule occurred at both bonds of sulfur with the radicals to form the corresponding thiols. This may be illustrated in the following way:



(5)

The secondary processes are the conversions of β-thionaphthol to naphthalene, decyl mercaptan to decene, and the latter to decane. In this more complex case where the sulfide molecule is cleaved both at the bond of sulfur with the naphthalene nucleus and at the bond of sulfur with the alkyl, it is possible to draw the conclusion that the bond of naphthalene in the β-position with sulfur is approximately equal in strength to the bond of sulfur with an alkyl radical. As pointed out previously, the latter bond occupies an intermediate position between the

strong bond of sulfur with a benzene nucleus and the weak bond of sulfur with naphthene radicals. An experiment with β-naphthyl cyclopentyl sulfide (4) confirmed that the bond of sulfur with a β-naphthyl radical is actually stronger than the bond of sulfur with a naphthene radical.

For clarity, we show scheme 6, where the broken lines denote the positions at which the bonds in the sulfides are ruptured when the latter are passed over an aluminosilicate catalyst. Scheme 6 shows that the bond of sulfur with a benzene nucleus is the strongest and is not ruptured in any of the cases we studied. The bond of sulfur with alkyl radicals and a β-naphthyl radical is stronger than the bond of sulfur with naphthene rings. In the light of our new data, the weakest bond is found to be that of sulfur with an α-naphthyl radical.

$$\begin{array}{ll} C_6H_5—S—C_{10}H_{21} & C_{10}H_{21}—S—C_6H_{11} \\ C_6H_5—S—C_5H_9 & \beta\text{-}C_{10}H_7—S—C_5H_9 \\ C_6H_5—S—C_6H_{11} & C_{10}H_{21}—S—\alpha\text{-}C_{10}H_7 \\ C_{10}H_{21}—S—C_5H_9 & C_5H_9—S—\alpha\text{-}C_{10}H_7 \end{array} \qquad (6)$$

EXPERIMENTAL

1. Synthesis of α-thionaphthol and its conversion on an aluminosilicate catalyst. α-Thionaphthol was synthesized by reduction of naphthalene-α-monosulfonyl chloride [4]. The latter was obtained by the reaction of naphthalene with chlorosulfonic acid [5]. For the preparation of naphthalene-α-monosulfonyl chloride, we used 143 ml of chlorosulfonic acid and 77 g of naphthalene. The weight of the crude naphthalene-α-monosulfonyl chloride was 50 g (36.7%). The m.p. was 65-67° (m.p. 68° [5]).

To a mixture of 65 g of zinc dust and 200 ml of water at 60° was added 50 g of naphthalene-α-monosulfonyl chloride, a further 10 g of zinc dust added, and the mixture heated at 70° for 20 min. Then 500 g of concentrated hydrochloric acid and 200 g of water were added. A further 50 g of zinc dust was introduced and the mixture heated on a water bath for 3 hr. The unreacted zinc dust was removed on a Buchner funnel and pressed out well with a stopper. The thionaphthol passed through the filter in the form of a yellow oil and was dissolved in ether and the zinc precipitate washed repeatedly with ether. The yield of α-thionaphthol was 23 g (72%). It had b.p. 143-144° (6 mm), $n^{20}D$ 1.6802, d^{20}_4 1.1607 [b.p. 152.5-153.5° (15 mm), d^{23}_4 1.1549 [6].

We studied the conversion of α-thionaphthalene on an aluminosilicate previously [1]. Only naphthalene (51.6%) was isolated from the catalyzate.

2. Synthesis of β-thionaphthol and its conversion on an aluminosilicate catalyst. β-Thionaphthol was synthesized by reduction of naphthalene-β-monosulfonyl chloride and the latter was obtained by treatment of sodium β-naphthalenesulfonate with phosphorus pentachloride [7]. From 275 g of sodium β-naphthalenesulfonate 243 g of PCl_5, and 46 g of PCl_3 we obtained 150 g (55.4%) of β-naphthalenesulfonyl chloride with m.p. 75-76° (m.p. 76° [7]).

The preparation of β-thionaphthol was based on Schroeter's procedure [8] for the reduction of β-tetralinsulfonyl chloride. A mixture of 48 g of β-naphthalenesulfonyl chloride, 200 ml of hot water and 48.6 g of zinc dust was heated on a boiling water bath for 1 hr, 200 ml of concentrated hydrochloric acid added, the mixture stirred on a boiling water bath for 6 hr, 20 g zinc dust added, and the mixture stirred on a salt bath (105-107°) for 4 hr. The white precipitate was collected by filtration and the β-thionaphthol distilled from it with steam superheated to 170°. The yield of β-thionaphthol was 27.4 g (80%). The m.p. was 79-80° (m.p. 80-81° [4]).

For a study of the catalytic conversions, 20 g of β-thionaphthol was passed over aluminosilicate in a stream of nitrogen at 300° with a space velocity of about 0.2. The evolution of hydrogen sulfide was observed. The solid catalyzate with a smell of naphthalene melted at 77°. On sublimation it yielded 8.5 g (53%) of naphthalene with m.p. 80°, whose picrate had m.p. 149° (literature data: naphthalene m.p. 80.2°[9], naphthalene picrate m.p. 150° [10]). No other compounds apart from naphthalene and hydrogen sulfide were detected in the catalyzate.

3. Synthesis of α-naphthyl decyl sulfide and its catalytic conversion. We previously described [11] the preparation of α-naphthyl decyl sulfide from potassium α-thionaphtholate and decyl bromide in 72% yield.

TABLE 1

Composition of Catalyzate from α-Naphthyl Cyclopentyl Sulfide

Substances	Weight		Boiling point	n_D^{20}	d_4^{20}	Literature data			
	in g	in % of catalyzate				boiling point	n_D^{20}	d_4^{20}	reference
Cyclopentanethiol	0.9	6.6	80—82° (100mm)	1.4880	0.9560	129—130° (745mm)	1.4880	0.9550	[12]
Naphthalene*	5.5	40.0	M.p. 80°	—	—	M.p. 80°	—	—	[9]
Dicyclopentyl sulfide	0.3	2.2	~116 (100mm)	1.5200**	0.9800**	134° (26mm)	1.5102	0.9726	[12]
α-Naphthyl cyclopentyl sulfide	1.0	7.3	172—174 (4mm)	1.6425	1.1201	***	—	—	
Tar	3.9	28.6	—	—	—	—	—	—	

*Melting point of picrate 150° (150° [10]).

**MR_D 52.8. $C_{10}H_{18}S$. Calculated 52.2.

***The constants of the starting α-naphthyl cyclopentyl sulfide are given below in the description of its synthesis.

The catalytic conversion of α-naphthyl decyl sulfide on aluminosilicate was also studied [1]; the catalyzate yielded naphthalene (36.6%), decyl mercaptan (13.1%), and decene (7.8%). The catalyzate did not contain thionaphthol.

4. Synthesis of α-naphthyl cyclopentyl sulfide and its catalytic conversion. The sulfide was obtained by the reaction of potassium α-thionaphtholate with cyclopentyl bromide. α-Thionaphthol (48 g) was added dropwise with stirring to a solution of 17 g of potassium hydroxide in 38 ml of alcohol at 80° and the mixture heated for 1 hr. While the mixture was stirred at the same temperature, 44.7 g of cyclopentyl bromide was added dropwise. The reaction mixture was heated for 2 hr at 90-95° and 1 hr at 120-130° and then poured into water, the sulfide extracted with ether, and the ether extract washed with 10% alkali solution to remove unreacted α-thionaphthol. The yield of α-naphthyl cyclopentyl sulfide was 31.5 g (45.6%). The b.p. was 168-168.5° (2 mm) and the compound had $n^{20}D$ 1.6419, d^{20}_4 1.1193.

Found %: C 78.83, 78.80; H 7.11, 7.04; S 13.91, 14.09. $C_{15}H_{16}S$. Calculated %: C 78.89; H 7.06; S 14.05.

α-Naphthyl cyclopentyl sulfide has not been described in the literature and was prepared for the first time.

For a study of the catalytic conversions, 22.7 g of α-naphthyl cyclopentyl sulfide was passed over aluminosilicate at 300° under the conditions we adopted [3]. The receiver was cooled with snow and salt to condense any cyclopentene that might have been formed. The weight of the catalyzate (a mixture of solid and liquid) was 13.7 g (60.3%) of the weight of the starting sulfide). The catalyzate was heated on a water bath in an apparatus with a distillation condenser to distil cyclopentene (b.p. 44°). None of the latter was found in the catalyzate. The catalyzate was then dissolved in ether and treated with 20% sodium hydroxide solution to extract thiols. Acidification of the alkaline extract yielded cyclopentanethiol. α-Thionaphthol was not detected. After removal of the ether, freezing the residue yielded naphthalene. Distillation of the liquid portion of the catalyzate yielded dicyclopentyl sulfide and the starting α-naphthyl cyclopentyl sulfide. In the flask remained 3.0 g of tar. The amounts of substances isolated from the catalyzate, their constants, and literature data are given in Table 1.

The hydrogen sulfide in the emergent gases was precipitated with sodium plumbite. The weight of PbS obtained was 17.7 g, which corresponds to 2.3 g of sulfur (72.6% of the sulfur of the starting sulfide).

TABLE 2

Composition of Catalyzate from β-Naphthyl Decyl Sulfide

Substances	Weight		Temperature		n_D^{20}	d_4^{20}	Literature data			
	(in g)	% wt. of catalyst	melting point	boiling point (pressure in mm)			boiling point	n_D^{20}	d_4^{20}	reference
Decene–decane fraction	1.8	4.2		56—57° (10)	1.4243	0.7362	Decene Decane	1.4214 1.4118	0.7408 0.7298	[13]
Decyl mercaptan	2.6	6		106—108 (10)	1.4599	0.8431	103° (9mm)	1.4576	0.8414	[3]
β-Thionaphthol	0.5	1.1	80°	143—146 (10)	—	—	*	—	—	
Naphthalene**	13.1	30.5	80	—	—	—	*	—	—	[9]
Higher fraction	3.6	8.5	—	170—270 (2)	1.5730	0.9705	—	—	—	—

*The constants of β-thionaphthol and naphthalene are given above.

**Melting points of picrate 148.5° (150° [10]).

5. Synthesis of β-naphthyl decyl sulfide and its catalytic conversion. This sulfide was obtained from 56 g of β-thionaphthol, 80 g of decyl bromide, and 19.6 g of potassium hydroxide dissolved in 68 ml of alcohol, by the procedure described above for the synthesis of α-naphthyl cyclopentyl sulfide. The yield of β-naphthyl decyl sulfide was 71.7 g (68%). It had b.p. 209-210° (2.5 mm) and m.p. 34-35°.

Found %: C 79.48, 79.66; H 9.43, 9.38; S 11.41, 11.11. $C_{20}H_{28}S$. Calculated %: C 79.93; H 9.39; S 10.68.

β-Naphthyl decyl sulfide has not been described in the literature and was prepared for the first time.

For a study of the catalytic conversions, two 30-g portions of β-naphthyl decyl sulfide were passed over aluminosilicate at 300° under the conditions we adopted [3]. After the first portion had been passed, the catalyst was regenerated [3]. The total weight of catalyzate was 42.9 g (71.5% of the weight of the starting sulfide). Naphthalene was isolated from the catalyzate (a mixture of liquid and solid) by freezing. Distillation of the liquid portion of the catalyzate yielded a decene-decane fraction (bromine number 52, which corresponds to 45.5% of decene), a small amount of naphthalene, decyl mercaptan, and β-thionaphthol. It was not possible to isolate individual compounds from the fraction with b.p. 170-237°. The amounts of substances isolated from the catalyzate, their constants, and literature data are given in Table 2.

The hydrogen sulfide in the emergent gases was precipitated with sodium plumbite. The weight of the PbS obtained was 25.6 g, which corresponds to 3.4 g of sulfur (52% of the sulfur of the starting sulfide).

6. Synthesis of β-naphthyl cyclopentyl sulfide and its catalytic conversion. This sulfide was prepared from 45 g of β-thionaphthol, 46 g of cyclopentyl bromide, and 16.8 g of potassium hydroxide dissolved in 140 ml of ethanol by the procedure described above for the synthesis of α-naphthylcyclopentyl sulfide. The yield of β-naphthyl cyclopentyl sulfide was 41.7 g (65%) and the compound had b.p. 187.5-188° (4 mm), $n^{20}D$ 1.6455, d^{20}_4 1.1052.

Found %: C 78.94, 78.94; H 6.97, 6.85; S 14.33, 14.33. $C_{15}H_{16}S$. Calculated %: C 78.89; H 7.06; S 14.05.

β-Naphthyl cyclopentyl sulfide has not been described in the literature and was obtained for the first time.

For a study of the catalytic conversion, 30 g of this sulfide was passed over aluminosilicate at 300° under the conditions we adopted [3]. The receiver was cooled with snow and salt to condense any cyclopentene that might have been formed. The weight of the catalyzate was 18.6 g (62% of the weight of the starting sulfide). The catalyzate was heated on a water bath in an apparatus with a distillation condenser. The liquid thus obtained

TABLE 3

Composition of Catalyzate from β-Naphthyl Cyclopentyl Sulfide

Substances	Weight		Boiling or melting point
	in g	in % of catalyzate wt.	
Cyclopentene•	1.9	10.2	44—45° (754 mm)
Naphthalene••	8.1	43.5	M.p. 80
β-Thionaphthol•••	2.9	15.6	M.p. 79—80
Tar	2.7	14.5	200—260 (2 mm)

•Found for cyclopentene: $n^{20}D$ 1.4226, d^{20}_4 0.7729 (b.p. 44.2° at 760 mm, $n^{20}D$ 1.4225, d^{20}_4 0.7720 [14]).

••Melting point of picrate 150° (150° [10]).

•••The constants of β-thionaphthol are given above.

was redistilled and found to be cyclopentene. The solid part of the catalyzate was washed with hot 20% alkali solution and water, dried, and sublimed. It was found to be naphthalene. Acidification of the alkaline extract yielded β-thionaphthol. The amounts of the substances isolated from the catalyzate, their constants, and literature data are given in Table 3.

The hydrogen sulfide from the emergent gases was precipitated with sodium plumbite. The weight of PbS was 26.5 g, which corresponds to 3.5 g of sulfur (84% of the sulfur of the starting sulfide).

SUMMARY

1. Isomeric α- and β-thionaphthols were passed over an aluminosilicate catalyst at 300°, when they behaved analogously and formed naphthalene and hydrogen sulfide.

2. When mixed α-naphthyl sulfides (α-naphthyl decyl sulfide and α-naphthyl cyclopentyl sulfide) were passed over aluminosilicate at 300°, the molecules were cleaved between the sulfur and the naphthalene nucleus with the formation of naphthalene and a mercaptan.

3. Under the same catalysis conditions, β-naphthyl cyclopentyl sulfide decomposed to β-thionaphthol and cyclopentene with rupture of the bond between the sulfur and the cyclopentane ring. With β-naphthyl decyl sulfide there was cleavage of the molecules both at the bond of sulfur with naphthalene and at the bond of sulfur with the decyl radical.

4. When mixed sulfides are passed over an aluminosilicate catalyst, the sulfide molecules are cleaved between the sulfur and the radicals and the bond of the sulfur with a benzene ring is the strongest. The bond between sulfur and alkyl radicals and a β-naphthyl radical is stronger than the bond of sulfur with naphthene rings. The bond of sulfur with an α-naphthyl radical was found to be the weakest.

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CATALYSIS OF DEUTERIUM EXCHANGE IN LIQUID HYDROGEN IODIDE BY IODINE

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Many solvents differing in acid–base and physical properties have been used in our laboratory for establishing the rules of isotopic exchange of hydrogen. Comparisons have been made of deuterium exchange in protophilic solvents such as liquid ammonia, anhydrous hydrazine, ethylenediamine, and ethanolamine [1], in amphoteric solvents such as water and alcohols (CH_3OH, C_2H_5OH, iso-C_3H_7OH, $HOCH_2CH_2OH$) [2], and in acidic solvents such as carboxylic acids• and liquid hydrogen halides. Data were obtained on deuterium exchange in hydrogen bromide [3-12], fluoride [13, 14], and chloride [15]. In this communication we describe experiments with the last of the hydrogen halides, namely, liquid hydrogen iodide. It was shown that deuterium exchange in it is catalyzed by iodine and an explanation is put forward for this phenomenon.

EXPERIMENTAL

Hydrogen iodide was synthesized in a quartz apparatus similar to that used for work with liquid deuterium bromide [16]. Part of the apparatus is illustrated in Fig. 1. A mixture of iodine vapor from heated reservoir 2 and hydrogen, freed from oxygen and moisture, was passed into furnace 3, which was filled with platinized asbestos and heated to 800°. The HI was freed from I_2 in traps 4 and 5, which were cooled with a mixture of solid CO_2 and acetone, and condensed in receiver 6, immersed in a Dewar vessel with liquid air. The unreacted hydrogen passed out from the system through seal 8. When about 150 g of HI had accumulated in 6, the tap was closed, a vacuum applied, and the HI distilled into trap 7, cooled to -45°, from which approximately 20-g portions were taken and condensed in measuring tube 9 and used to fill tube 10, which was sealed to the apparatus and contained thin-walled ampoules with the substance investigated and catalyst (iodine). The hydrogen iodide was frozen with liquid air, carefully purified nitrogen admitted to the system, and the tube connected to the atmosphere through the bubble counter 12 and the drying system 11 and then sealed off at the constriction. The tube was then placed in a thermostat (25 ± 0.2°). The HI vapor pressure crushed the ampoules with the hydrocarbon and catalyst and these substances dissolved with mixing. The weight of HI usually varied over the range 17-21 g, the toluene sample weighed 0.20-0.25 g, biphenyl 0.16-0.19 g, and iodine 0.002-0.09 g. There was 50-70 moles of HI to 1 mole of toluene and 100-150 moles of HI to 1 mole of biphenyl. In experiments without catalyst the solution was first colorless and then gradually acquired a pink color due to photochemical decomposition of HI. In experiments with iodine added, the solution varied from pink to violet and at low temperature was brown. To stop the exchange reaction, the reaction mixture was frozen with liquid air, the solvent evaporated, and an aqueous solution of alkali added to remove I_2 and residual HI. After the hydrocarbon had been separated and purified, the constants of the substance and the deuterium concentration in it were determined.

In the work we used the same preparations of monodeutero hydrocarbons (which were synthesized by E. N. Yurygina) as in [10]. Some of them were diluted with normal hydrocarbon. When dissolved in liquid HI,

•See brief communication [45].

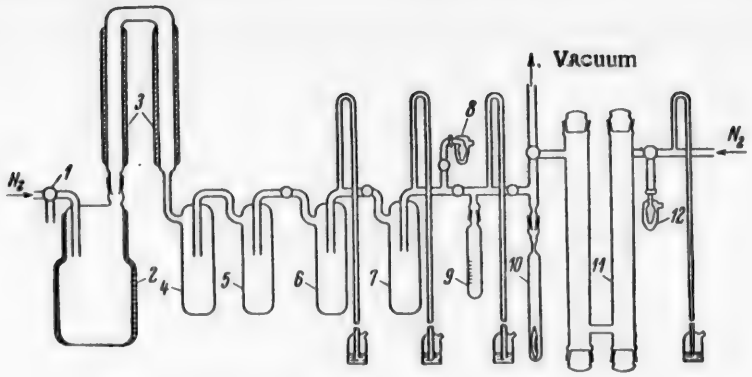

Fig. 1. Apparatus for the synthesis and purification of HI.

naphthalene changed chemically quite quickly. Therefore, only preliminary experiments were carried out with it and the bulk of the work was carried out with isomers of monodeuterotoluene and monodeuterobiphenyl, which were quite resistant to liquid HI.

The rate constants of the exchange reactions (in sec^{-1}) were calculated from a first order equation as described in [10]. In the introduction of corrections, it was assumed that the distribution coefficient for deuterium between C-H and H-I bonds $\alpha = 3.5$ [17].

RESULTS OF MEASUREMENTS

Table 1 gives a summary of the results. We adopted the following symbols: τ for the duration of an experiment in hr, C_{ArD} for the number of moles of hydrocarbon per mole of HI, C_{I_2} for the iodine concentration in moles per mole of HI, C^0_W for the deuterium concentration in the water from combustion of the substance before the experiment (in at. %), C_W for the same at the end of the experiment, $\underline{k}$ for the rate constant of deuterium exchange, $k' = k/C_{I_2}$ for the specific rate constant relative to the I_2 concentration in solution, and $C = C_{ArD}/C_{I_2}$.

In order to obtain the rate constants of deuterium exchange with liquid HI in the absence of iodine, a graph was plotted of the rate constants (sec^{-1}) for each of the substances investigated against the iodine concentration in the solution and extrapolated to zero concentration. In this way, the following values for the rate constants of deuterium exchange were obtained:

p-D-biphenyl: $4 \cdot 10^{-6}$; o-D-biphenyl: $1 \cdot 10^{-6}$
p-D-toluene: $4 \cdot 10^{-6}$; o-D-toluene: $2 \cdot 10^{-6}$

The spectra of solutions of iodine in liquid HI were plotted at room temperature by the procedure described previously [18] on an SF-4 spectrophotometer. The layer thickness of the quartz cell was 0.11 cm. The absorption coefficient of iodine over the concentration range of $3\text{-}8 \cdot 10^{-3}$ mole of I_2 / liter obeyed the Lambert-Beer law. For the maximum on the curve (λ 500 mμ), the molar absorption coefficient $\epsilon = 1.0 \cdot 10^3$. Liquid HI absorbs light weakly at 360 mμ; strongly at 300 mμ. In calculation of the absorption coefficient of an I_2 solution, allowance was made for the light absorption by the solvent. The latter prevented us from establishing the short-wave absorption maximum of iodine if it existed. Figure 2 shows absorption curves of solutions of I_2 in liquid HI (curve 3), C_6H_6 (curve 2), and CCl_4 (curve 1). Solutions of I_2 in HI and C_6H_6 absorb light in the spectral region (360-400 mμ) where there is no appreciable absorption of light by a solution in CCl_4. Therefore, it is possible that there is a weak interaction between iodine and hydrogen iodide, for example, and equilibrium of the type

$$I_2 + HI \rightleftharpoons HI \cdot I_2 \qquad (A)$$

The specific electrical conductivity of liquid HI was measured at -44° in a cell with unplatinized platinum electrodes (cell constant c = 0.024) with an ac bridge (frequency 2000 cps), constructed in our institute under the direction of V. E. Kazakevich. An ÉO-7 oscillograph was used as a null instrument. The electrical conductivity of liquid HI was found to be less than $2 \cdot 10^{-8}$ ohm^{-1} cm^{-1}, which was the sensitivity limit of the measuring instrument. The electrical conductivity did not increase appreciably with the solution of iodine ($5 \cdot 10^{-2}$ mole of I_2/ mole of HI) or with the addition of mesitylene or hexamethylbenzene to this solution.

TABLE 1

Results of Experiments on Deuterium Exchange with Liquid HI

№	$C_{ArD} \cdot 10^3$	$C_{I_2} \cdot 10^4$	C^0_W	C_W	τ	$k \cdot 10^4$	$k' \cdot 10^3$	C
				p-D-Toluene				
1	1.4	—	10.80	5.86	45	4.0	—	—
2	1.4	—	10.80	5.90	45	4.0	—	—
3	1.7	—	5.50	3.05	43	4.0	—	—
4	1.7	—	5.50	3.02	43	4.0	—	—
5	1.6	0.6	5.60	3.43	28	5.2	8.7	270
6	1.9	1.2	5.60	2.86	22	9.2	7.7	160
7	1.8	2.0	5.60	3.16	14	12	6.0	90
8	1.8	3.5	5.50	2.88	8	24	6.9	51
9	1.7	5.9	5.50	2.70	5	43	7.3	29
10	1.9	6.9	5.60	3.23	3	55	8.0	28
11	1.8	10	5.60	3.02	2	92	9.1	18
12	2.2	12	5.60	2.94	1.5	130	10.8	18
				o-D-Toluene				
13	1.6	—	5.50	3.65	64	2.1	—	
14	1.6	1.1	5.50	2.96	50	4.0	3.6	150
15	1.9	2.2	5.50	3.09	30	6.4	2.9	86
16	1.6	2.6	5.50	3.32	23	7.1	2.7	62
17	1.9	3.9	5.50	2.43	24	12	3.1	49
18	1.6	5.8	5.50	2.76	12	19	3.3	28
19	1.5	11	5.50	2.68	5	47	4.3	14
20	1.8	14	5.50	3.18	3	61	4.4	13
21	1.8	25	5.50	2.21	2	160	6.4	7
				p-D-Biphenyl				
22	0.75	—	8.10	4.27	45	4.2	—	—
23	0.63	0.8	8.10	3.97	28	8.6	10.8	79
24	0.67	2.1	8.10	4.44	12	15	7.2	32
25	0.86	3.8	8.10	4.93	6	25	6.6	23
26	0.71	12	8.10	5.08	1.5	91	7.6	6
				o-D-Biphenyl				
27	0.71	1.8	7.80	4.76	45	3.5	2.0	39
28	0.82	3.4	7.80	5.19	23	5.6	1.7	24
29	0.75	5.2	7.80	4.27	25	7.9	1.5	14
30	1.1	7.8	7.80	4.76	12	14	1.8	14
31	0.24	11	7.80	5.12	6	20	1.8	2
32	0.83	12	7.80	5.40	5	23	1.9	7
33	0.82	17	7.80	5.01	4	36	2.1	5

A solution of iodine with mesitylene had a red-violet color and a corresponding solution with hexamethylbenzene had a red-brown color, which was probably explained by the formation of a molecular compound between the hydrocarbon and iodine:

$$ArH + I_2 \rightleftharpoons ArH \cdot I_2 \qquad (B)$$

The electrical conductivity measurements indicated the absence of appreciable ionization in these systems.

Hydrogen iodide is readily decomposed by the action of light. Judging by spectrophotometric measurements, under our experimental conditions the iodine concentration reached $1 \cdot 10^{-4}$ mole of I_2/mole of HI.

DISCUSSION OF RESULTS

In experiments with biphenyl, over a considerable range of iodine concentrations (C_{I_2} = 2-17 · 10^{-4} mole per mole of HI) there was direct proportionality between the rate constants and the iodine concentrations. The specific rate constant k' remained constant to within 20%. Its deviations in the region of low iodine concentrations are explained by partial decomposition of HI with the liberation of I_2 in an amount commensurate with

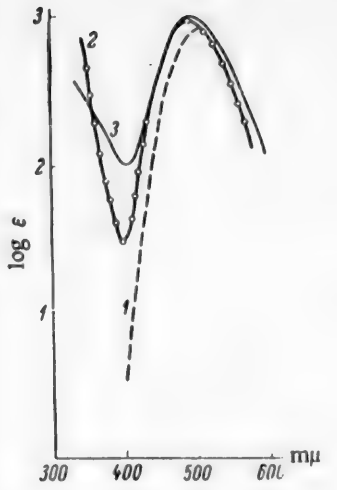

Fig. 2. Absorption spectra of solutions: 1) in CCl_4; 2) in C_6H_6; 3) in liquid HI.

that added. With excess hydrocarbon, the value of k' did not change substantially, regardless of the ratio between the iodine and hydrocarbon concentrations (C). The reason for the lack of constancy of k' in experiments with toluene has not been explained.

The systems in which the exchange reactions occurred consisted of three components: HI (solvent), ArD (substrate), and I_2 (catalyst). A number of equilibria are possible in it. The literature contains detailed studies of equilibria of type (B) (see [19] and reviews [20, 21]) and there are reports [22] of the formation of a hydrogen bond between ArH and HI molecules:

$$ArH + HI \rightleftarrows ArH \ldots HI \qquad (C)$$

We consider that the catalytic activity of iodine in deuterium exchange in liquid HI is caused by the existence of the equilibrium

$$ArD + HI + I_2 \rightleftarrows ArD \ldots H{-}I \cdot I_2 \qquad (D)$$

(We cannot exclude the possibility that instead of ArD, its complex with iodine, $ArD \cdot I_2$, participates in the equilibrium.) It is probable that the reaction is limited by polarization of the H-I bond and the complex ions I_3^- do not arise. In any case, as the electrical conductivity measurements show, the concentration of free ions is very low. Equilibrium (D) is analogous to reactions which have been thoroughly studied in which, in addition to a hydrogen halide and an aromatic hydrocarbon, there is also involved an aluminum or boron halide or another electron-acceptor reagent [23-27], for example:

$$ArD + HHal + AlHal_3 \rightleftarrows ArD \ldots H^{\delta+}{-}AlHal^{\delta-} \qquad (E)$$

In such systems there is isotopic exchange of hydrogen [3, 8, 9, 14, 28, 29]. The efficiency of the catalyst depends on the degree to which it polarizes the H-Hal bond [30-32].

For further support for the proposed explanation of the catalysis of deuterium exchange by iodine, let us turn to the electrophilic replacement of hydrogen in aromatic hydrocarbons (for example, bromination), whose mechanism has much in common with the mechanism of acid hydrogen exchange [31].

Bromination is catalyzed by metal halides and iodine ($AlBr_3 > FeBr_3 > I_2$) (see [33]). The opinion has long been held [34] that their role consists of polarization of the bromine molecule:

$$ArH + Br_2 + I_2 \rightleftarrows ArH \ldots Br^{\delta+}{-}Br^{\delta-} \cdot I_2 \qquad (F)$$

The positively charged bromine reacts with the hydrocarbon at a position with a high electron density. In accordance with this conclusion, E. A. Shilov and N. I. Konyaev [35] showed that a brominating agent is more active the more strongly it is polarized. The series is headed by the bromine cation Br^+, the rate of bromination by which is almost 1500 times greater than the rate of bromination of the same hydrocarbon by molecular bromine, as bromine molecules polarize each other very weakly:

$$ArH + Br_2 + Br_2 \rightleftarrows ArH \cdot Br^{\delta+}{-}Br^{\delta-} \cdot Br_2 \qquad (G)$$

The halogenation rate is also increased by an increase in the nucleophily of the hydrocarbon [36, 37].

Thus, the catalytic activity of iodine in the reactions compared, namely acid deuterium exchange and bromination, is explained analogously: By polarizing the hydrogen halide molecule, iodine facilitates the approach of the proton to the hydrocarbon molecule, while in bromination it polarizes the bromine molecule and promotes the conversion of the molecular halogen into the ionic state.

Let us return to an examination of the rate constants of deuterium exchange between hydrocarbons and HI, which were obtained by extrapolation of curves to zero iodine concentration. Let us compare them with the rate constants of deuterium exchange between the same hydrocarbons and liquid HBr [7, 10] and HF [14]. The factors of the partial rate of deuterium exchange with liquid HF for deuteroisomers of a hydrocarbon labeled in the ring

TABLE 2

Comparison of Rate Constants of Deuterium Exchange with Various Hydrogen Halides at 25° (sec^{-1})

Hydrocarbon	HI	HBr	HF
o-D-Toluene	$2 \cdot 10^{-6}$	$5 \cdot 10^{-5}$	$> 2 \cdot 10^{-2}$
p-D-Toluene	$4 \cdot 10^{-6}$	$2 \cdot 10^{-4}$	—
o-D-Biphenyl	$1 \cdot 10^{-6}$	$3 \cdot 10^{-5}$	—
p-D-Biphenyl	$4 \cdot 10^{-6}$	$1 \cdot 10^{-4}$	—
α-D-Naphthalene . .	$(5 \cdot 10^{-5})$	$2—3 \cdot 10^{-3}$	—

TABLE 3

Constants of Hydrogen Halides

Substance	Dielectric constant	$\mu \cdot 10^{18}$	K_{H_2O}
HF	175 (—73°)	1.91	$6 \cdot 10^{-4}$
HCl	9 (—90°)	1.04	$10^{6}—10^{7}$
HBr	6 (—80°)	0.79	$10^{8}—10^{9}$
HI	3 (—50°)	0.38	$10^{9}—10^{11}$

with the isotope should differ little from each other [31]. Therefore, it can be assumed provisionally that the mean rate constant obtained in [14] equals k_{ortho}. Table 2 gives the rate constants of exchange with different hydrogen halides. With liquid HI, as with liquid HBr, the hydrogen atoms of toluene and biphenyl in the para position exchange more rapidly than those in the ortho position.

With liquid HI the exchange reactions at 25° proceed more slowly by a factor of 25-50 than with liquid HBr, and with the latter they are approximately 3 orders slower than with HF. (The rate constants of deuterium exchange of benzene with HBr and HF differ even more: $K_{HBr} = 5 \cdot 10^{-8}$; $K_{HF} = 1 \cdot 10^{-3}$ sec^{-1}). Due to the experimental complexity of kinetic measurements with liquefied hydrogen halides, the parameters of the Arrhenius equation were not determined. This hampers the discussion of differences in the kinetics of deuterium exchange with liquid hydrogen halides.

Aromatic hydrocarbons are partly ionized in liquid hydrogen fluoride [25]. There is probably considerable polarity of the bond arising in the transition state, depending on the strong acidity of liquid HF, the high polarity of its molecules, and the high dielectric constant (Table 3). This gives us the reason for the rapid hydrogen exchange, whose rate constant is 3-5 orders higher than the rate constants of exchange reactions with other hydrogen halides. However, as Mackor noted [38], even in liquid hydrogen fluoride, which has an outstanding ionizing capacity, a considerable role may be played by associative processes as, for example, in hydrogen exchange with benzene. They stand out in exchange reactions with the other hydrogen halides, which differ from HF in a low dielectric constant and considerably less polarity of the molecules. In accordance with this, we did not detect an appreciable change in the electric conductivity of liquid hydrogen iodide not only with the solution of an aromatic hydrocarbon, but also when an electrophilic reagent was added to its solution.

The rate of hydrogen exchange depends on the acidity of the medium. In much work [38, 40] it has been established that there is a linear relation between the logarithm of the rate constant of an exchange reaction and the acidity function H_0 of the solution in which the reaction occurs. There are no data on the acidity of liquid HCl, HBr, and HI. It is normally considered that the acidity of hydrogen halides increases in parallel with an increase in the atomic weight of the halogen. This conclusion is in agreement with the values of their ionization constants in water K_{H_2O} [41] and data on the acidity of nonaqueous solutions. How far these comparisons are from the truth on going from dissociation constants of acids in solution to an assessment of the strength of acids

in an anhydrous liquid state is shown, for example, by the fact that in aqueous solution HF is quite a weak acid whose dissociation constant $K_{H_2O} = 6 \cdot 10^{-4}$, i.e., 10-15 orders below the dissociation constants of the other hydrogen halides (from a very approximate assessment), while the acidity function of liquid hydrogen fluoride differs little from H_0 for 100% sulfuric acid [42]. The values of H_0 for other hydrogen halides are not available. Their determination is difficult not only from the experimental point of view, but also for fundamental reasons. In the establishment of acidity scales in H_0 units, it is postulated that the ratio of the acidity coefficients of any electrically neutral base and the corresponding acid is constant. This assumption is justified only in solutions of acids with a high dielectric constant and is not true in media with a low dielectric constant.

In previous work of the laboratory [43] it was shown that in addition to the protolytic activity of the reagents, other factors affect hydrogen exchange. In comparing the rates of exchange reactions with liquid HI and HBr it should be remembered that the dielectric constant of HI is very low and that HI molecules are the least polar (Table 3). In addition, proton magnetic resonance measurements [44] have shown the anomalously high association of molecules in liquid HI in comparison with liquid HBr and HCl. It is possible that a combination of these factors explains the lower rate of deuterium exchange with HI than with HBr.

We would like to thank E. N. Yurygina for providing preparations of deuterated hydrocarbons.

SUMMARY

1. The rate of deuterium exchange in isomers of monodeuterotoluene and monodeuterobiphenyl with liquid hydrogen iodide in the presence of various amounts of iodine was established, the absorption spectra of solutions of I_2 in HI were determined, and the electrical conductivity of the solutions and also solutions containing polymethylbenzenes was measured.

2. Iodine catalyzes the exchange reaction due to polarization of the H-I bond in the complex formed in the ternary system aromatic hydrocarbon–hydrogen iodide–iodine.

3. The rate of hydrogen exchange with liquid hydrogen halides was compared with the properties of the latter.

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ISOMERIC CONVERSIONS OF ALKYLNAPHTHALENES

III. MECHANISM OF ISOMERIZATION OF MONOMETHYLNAPHTHALENES*

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We previously showed [2] that when the vapor of 1- and 2-methylnaphthalenes is passed over an aluminosilicate catalyst at 270° and above, there are reversible interconversions of these isomers. On reaching equilibrium, the monomethylnaphthalene fraction contained ~ 70% of the 2-methyl isomer.

Up to now isomeric conversions of alkylaromatic compounds in the presence of catalysts ($AlCl_3$, $AlBr_3$, BF_3-HF, aluminosilicate, etc.) have been studied largely on the example of benzene derivatives. The first investigators in this field [3, 4] considered that the isomerization of di- and polyalkylbenzenes is due to an intermolecular transfer of alkyl groups, which may be illustrated by the following scheme for our case.

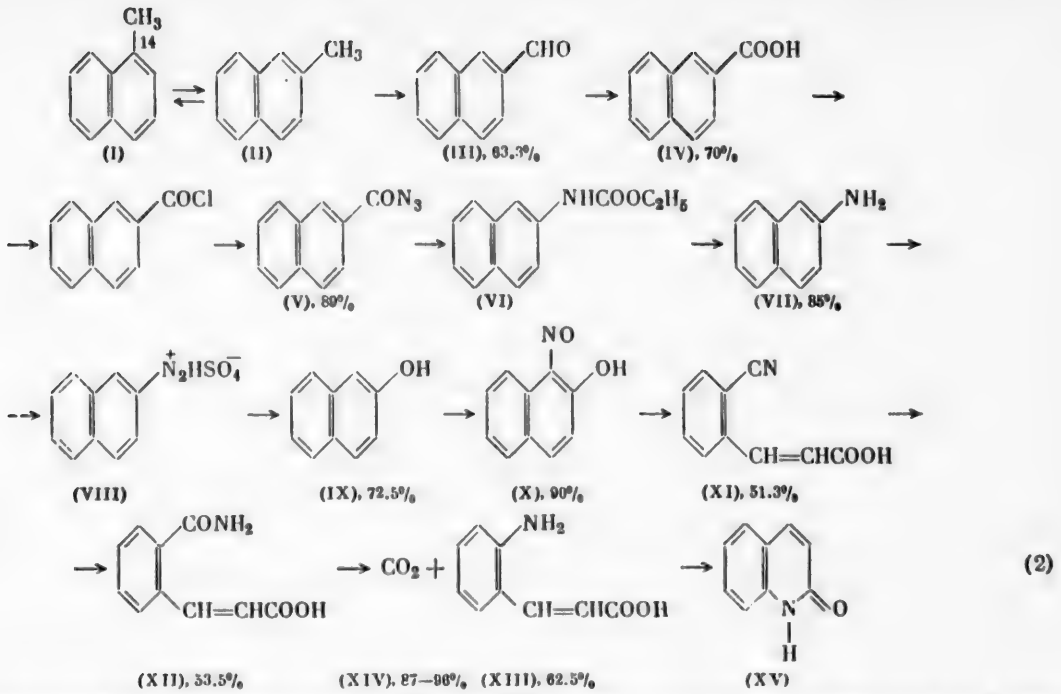
$$1\text{-}CH_3C_{10}H_7 + x\text{-}CH_3C_{10}H_7 \rightleftarrows C_{10}H_8 + C_{10}H_6(CH_3)_2 \rightleftarrows 2\text{-}CH_3C_{10}H_7 + y\text{-}CH_3C_{10}H_7 \quad (1)$$
$$x \text{ and } y = 1 \text{ or } 2$$

However, data were later obtained which indicate that the isomerization of alkyl derivatives of the benzene series is mainly connected with an intramolecular migration of an alkyl group. These data include the possibility of isomerization in a number of cases under conditions where disproportionation processes are practically impossible [5-7] and also the "stepwise" nature of the migration of the alkyl group [8, 9]. The latter means that the meta isomer is first formed from an ortho disubstituted benzene and only then does the para isomer begin to appear, i.e., in each individual act of the migration an alkyl group is transferred no further than to the neighboring carbon atom of the nucleus.

In the case of monomethylnaphthalenes, as for benzene derivatives, the isomerization proceeds more readily than disproportionation. At low temperatures (270-300°) under conditions where the ratio of isomers in the monomethylnaphthalene fraction approaches equilibrium, the yield of the naphthalene fraction was only 3-5% in our experiments [2]. This indicates that the isomerization of alkyl derivatives of naphthalene evidently proceeds largely intramolecularly and not according to scheme (1). However, this problem can only be solved conclusively if it is possible to show that in the isomerization of monomethylnaphthalenes a methyl group migrates to a neighboring carbon atom of the nucleus.

For this purpose we studied the isomerization of 1-^{14}C-1-methylnaphthalene (I), which was synthesized previously [1]. It was found that when the isomerization was carried out on an aluminosilicate catalyst at 320° in a stream of hydrogen chloride, 1-^{14}C-1-methylnaphthalene formed largely 1-^{14}C-2-methylnaphthalene. The content of the latter in the x-^{14}C-2-methylnaphthalene (II) obtained by isomerization was determined by removal of the carbon atom in position 1 from the molecule and comparison of the radioactivity of this atom and the rest of the molecule. The 1-C atom was removed as a result of the following series of conversions.

*See [1] for communication II.



(2)

By treatment with selenium dioxide at 220° [10], x-^{14}C-2-methylnaphthalene was converted into 2-naphthaldehyde (III) and the oxidation of this with potassium permanganate in aqueous pyridine• yielded 2-naphthoic acid (IV). By means of the Curtius reaction, the latter was converted through the azide (V) into the urethan (VI) [12], cleavage of which to 2-naphthylamine (VII) was accomplished by heating with potassium hydroxide in diethylene glycol at 165-175° (cf. [13]). Decomposition of the diazonium sulfate was used to replace the amino group in (VII) by a hydroxy group. The 2-naphthol (IX) thus obtained was then converted to 1-nitroso-2-naphthol (X) [14].

The C_1-C_2 bond of the naphthalene nucleus was cleaved by rearrangement of (X) into cis-o-cyanocinnamic acid (XI) by the action of p-toluenesulfonyl chloride in an alkaline medium [15]. By boiling with dilute hydrochloric acid [16], (XI) was then converted into trans-o-carbamidocinnamic acid (XII) and degradation of this by the Hofmann reaction yielded trans-o-aminocinnamic acid (XIII) and carbon dioxide (XIV). The latter contained the carbon atom from position 1 of the x-^{14}C-2-methylnaphthalene molecule. In order to ensure that the radioactivity of the trans-o-aminocinnamic acid (XIII) actually belonged to this compound and was not caused by impurities, this acid was converted to the carbostyril (XV) by boiling with dilute hydrochloric acid [17].

The results of measuring the radioactivity of (XII), (XIII), (XIV), and (XV) are given in the table and show that 94.5%•• of the 2-isomer obtained by isomerization of 1-^{14}C-1-methylnaphthalene was 1-^{14}C-2-methylnaphthalene.

This means that at least 92.6%••• of the molecules of 1-methylnaphthalene were isomerized under the given conditions to 2-methylnaphthalene without the intermediate formation of naphthalene, since with the migration of a methyl group by disproportionation (scheme 1) there should be formed an equimolecular mixture of 2-methylnaphthalenes labeled with radiocarbon in positions 1, 4, 5, and 8.

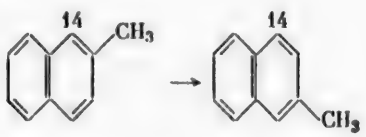
The results obtained leave no doubt but that the isomerization of monomethylnaphthalenes in the vapor phase over an aluminosilicate catalyst proceeds practically completely by an intramolecular mechanism. The retention of a small part of the radioactivity by the trans-o-aminocinnamic acid (XIII) is the result of either partial (7.4%) isomerization according to scheme (1) or further conversion of 1-^{14}C-2-methylnaphthalene into 1-^{14}C-3-methylnaphthalene.

•The procedure was based on that proposed for the oxidation of 2-nitro-4-chlorotoluene [11].

••100-$\frac{1}{2}$ (5.4 + 5.7) = 94.45.

•••100 - $\frac{4}{3}$ [$\frac{1}{2}$ (5.4 + 5.7)] = 92.6.

Compound	Radioactivity	
	μC/mole	%
o-$C_6H_4(CONH_2)CH{=}CHCOOH$ (XII)	4025 ± 2	100
CO_2 (XIV)	3917 ± 20	97.3
o-$C_6H_4(NH_2)CH{=}CHCOOH$ (XIII)	230 ± 5	5.7
$C_6H_4(NH)CH{=}CHCO$ (XV)	216	5.4

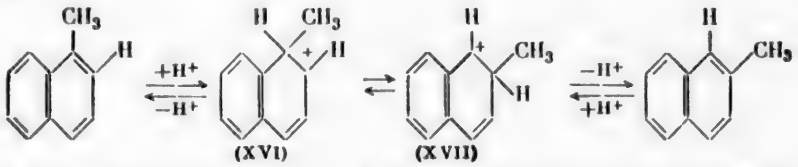


(3)

It should be emphasized that if the transfer of a methyl group from position 2 to position 3 occurs, then it is only to a small extent, as follows from a comparison of the radioactivities of the carbon dioxide (XIV) and the residue to the 2-methylnaphthalene molecule (XIII and XV). This is yet another argument in favor of the repeatedly expressed opinion on the very considerable localization of double bonds in the naphthalene molecule and this results in the difference between the C_1-C_2 and C_2-C_3 bonds [18-20].

We previously observed an analogous picture in the isomerization of 1-^{14}C-1-chloronaphthalene [21].

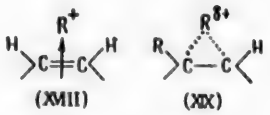
On the basis of contemporary ideas on the isomerization of alkyl derivatives of the benzene series [22], the intramolecular mechanism of monomethylnaphthalene isomerization may be represented in the general form in the following way.



(4)

According to this mechanism, the first stage of the isomerization process is the addition of a proton to the methylnaphthalene molecule with the formation of the corresponding σ-complex (XVI) or (XVII).• Though hydrogen chloride accelerates the isomerization, it is not essential to the process [2] and therefore the acidic centers of the aluminosilicate should be regarded as the proton source, the more so as the acid present in the aluminosilicate structure is very strong [23]. In the σ-complex formed there is transfer of the methyl group to the neighboring carbon atom, bearing a positive charge, to form an isomeric σ-complex.

Recent investigations (see [22]) have shed light on the formation of σ-complexes, but this is not true, however, of their rearrangement. The displacement of the alkyl group in the carbonium ions $>C(R)-C^+<$ to the positively charged carbon atom is characteristic of a whole series of conversions (pinacolin rearrangement, the rearrangements of Dem'yanov, Wagner, Nametkin, etc. [24]) but up to now both the reason and the mechanism have remained unknown (cf. [25]). Let us assume that during the transfer, the alkyl group passes through a state of binding to the electron pair of the π-bond (XVIII) or through a state of binding to the two carbon atoms (XIX).



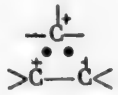
See [26] for the distinction between such structures.

• The carbonium ions (XVI) and (XVII) are undoubtedly only part of the reaction complex in which the anionoid center of the catalyst also participates.

In the first case it is also necessary to assume that (XVIII) is a "localized" π-complex [9] in contrast to the "delocalized" π-complex of Dewar (see [22], p. 401), in which the electrophilic group R^+ may be transferred freely along the edge of the π-electron cloud of the molecule. Otherwise, it would be quite difficult to explain the "stepwise" nature of the migration of the alkyl group.• The possibility of the existence of two types of π-complexes differing only in the degree of binding of the electrophilic group has not been demonstrated practically. Therefore, in adopting complex (XVIII) as the intermediate compound or the transition state it is necessary to consider available ideas on the nature of a "delocalized" π-complex. Furthermore, since isomerization may occur without simultaneous dealkylation and disporportionation, it is necessary to assume that in the "localized" π-complex (XVIII) the bond of the electrophilic residue R^+ with the pair of π-electrons is quite strong. The need for making all the additional assumptions given above forces one to treat the hypothesis on the passage of the migrating complex through a state of π-bonding (XVIII) with great caution.

The second hypothesis, which assumes the formation of the bridge structure (XIX) during migration of the alkyl group, also contains arbitrary elements. In particular, this concerns the direction of the bonds denoted by broken lines.

It seems to us that in both cases there is a one-sided approach to the problem. It would be more accurate to formulate the problem in the following way: At the moment of migration, the alkyl group passes through some state corresponding to an intermediate compound or transition state (the latter is more probable), the distribution of electron density in which is determined by the behavior of the two electrons in the field of the three positively charged atoms.



Ideas on three-centered orbitals apparently should give definite help in solving the problem of the electron density in such a state.

EXPERIMENTAL ••

1-^{14}C-1-Methylnaphthalene. See [1] for the preparation of this compound. The sample used had b.p. 108-110° (at 12 mm). B.p. 111° at 12 mm is reported in the literature [28] for 1-methylnaphthalene.

Isomerization of 1-^{14}C-1-methylnaphthalene and isolation of x-^{14}C-2-methylnaphthalene. 1-^{14}C-1-Methylnaphthalene was isomerized in the apparatus described previously [21]. The isomerization catalyst used was synthetic, tableted aluminosilicate, containing 30% aluminum oxide, 65.5% silica, and 0.5% iron oxide.••• The amount of catalyst was 9.1 g, the isomerization temperature 320-323°, and the hydrogen chloride input rate 30 ml/min. Over a period of 3.25 hr, 7.23 g of 1-^{14}C-1-methylnaphthalene (activity 18.2 mC/mole) was passed through the column. The catalyzate yield was 7.0 g (96.8%).

The pale yellow catalyzate was dissolved in 10 ml of ether, washed with water, and dried over anhydrous calcium chloride. The oil (6.85 g) remaining after evaporation of the ether had a solidification point of -2°. The oil was dissolved in 10 ml of anhydrous alcohol and cooled to -30°.

The x-^{14}C-2-methylnaphthalene precipitated was collected by filtration. Subsequent cooling of the filtrate to a lower temperature (finally to -60°) made it possible to isolate more of the 2-isomer. The total amount of x-^{14}C-2-methylnaphthalene thus obtained was 2.48 g.

In order to achieve a more complete separation, 1.05 g of unlabeled 2-methylnaphthalene •••• was dissolved in the remaining filtrate and the solution again cooled. After three such operations we obtained a further 3.71 g of x-^{14}C-2-methylnaphthalene with a lower radioactivity.

•For the same reason it is hardly possible to assume that in the isomerization of alkylaromatic compounds a complex is formed in which the migrating group is above the plane of the aromatic ring and bound simultaneously to all the π-electrons (see [27]).

••S. A. Kabanova and N. A. Morozova assisted in the development of the procedure for the conversion of 2-methylnapththalene to 2-naphthol.

•••We isomerized 1-^{14}C-1-chloronaphthalene [21] on a catalyst containing 12.7% aluminum oxide, 82.1% silica, and 0.3% iron oxide.

••••It was purified by recrystallization from methanol and had m.p. 34.5-35.0°.

The whole of the product obtained (6.19 g) was recrystallized from 12 ml of anhydrous alcohol (cooled to -30°) and to decrease the loss of x-^{14}C-2-methylnaphthalene in this case, unlabeled 2-methylnaphthalene was added to the filtrate (two portions of 1.00 g). We obtained a total of 7.09 g of a white crystalline substance with m.p. 32.0-33°. M.p. 34.4° is reported in the literature [29] for 2-methylnaphthalene.

2-Naphthaldehyde. x-^{14}C-2-methylnaphthalene (7.09 g) and 10 g of naphthalene were placed in a flask with a long neck and a stirrer on a metal bath.

With the bath temperature raised to 220°, 5.51 g of freshly prepared [30] and sublimed selenium dioxide was added to the mixture over a period of 35 min. The melt thereupon boiled and gradually became red. After the selenium dioxide had been added, stirring was continued for a further 5 min and then the reaction mixture was cooled and treated with 80 ml of ether. The undissolved red-brown residue was removed by filtration and washed with a further 40 ml of ether. The dark brown ether solution was transferred to a two-necked flask fitted with a reflux condenser, a dropping funnel, and a stirrer and a solution of 23 g of sodium hyposulfite in 35 ml of water was added with stirring. After a few minutes, a slightly yellowish precipitate of the bisulfite compound of 2-naphthaldehyde began to form.

The suspension was stirred for 1.5 hr at ~ 20° and left overnight. On the following day the ether layer was decanted and the remaining suspension washed with ether (6 portions of 45 ml each) by decantation. Then 200 ml of 15% sodium carbonate solution at 80° was carefully added to the suspension with stirring. Toward the end of the addition, the precipitate of bisulfite compound disappeared and a brown oil appeared on the surface of the solution. The mixture was heated to boiling and then cooled, and the crystallized oil extracted with ether (4 portions of 30 ml each). The extracts were dried with anhydrous sodium sulfate and the ether removed to yield 4.92 g (63.3%) of pale brown 2-naphthaldehyde.

2-Naphthoic acid. Over a period of 1.25 hr, a solution of 5.9 g of potassium permanganate in 100 ml of water was added to a solution of 4.92 g of unpurified 2-naphthaldehyde in 65 ml of pyridine in a two-necked flask fitted with a stirrer, reflux condenser, and dropping funnel and heated on a water bath. The reaction mixture was stirred for a further 20 min and then cooled to 50°. The manganese dioxide precipitate was removed by filtration and washed with 100 ml of boiling water. With a bath temperature of 115-120°, 140 ml of a pyridine-water mixture was distilled from the filtrate. The addition of 15 ml of concentrated hydrochloric acid to the remaining aqueous solution precipitated 2-naphthoic acid.

The weight of dry acid was 3.79 g (70.0%) and it had m.p. 178-181°. M.p. 185-186° is reported in the literature for 2 naphthoic acid (see [28], p. 4021).

Azide of 2-naphthoic acid. To a solution of 3.79 g of 2-naphthoic acid in 25 ml of anhydrous benzene in a flask with a reflux condenser was added 4.60 g of phosphorus pentachloride. When the evolution of hydrogen chloride slackened, the mixture was heated on a water bath to 60° and kept at this temperature for 15 min. The benzene was removed in a water-pump vacuum and to the residue was added 15 ml of benzene, and the mixture distilled. The addition and distillation of benzene (to remove volatile phosphorus compounds) was repeated twice more. The 2-naphthoyl chloride (brown oil) remaining in the flask was dissolved in 30 ml of acetone; the solution was filtered to remove turbidity, cooled to 3°, and treated with a solution of 2.3 g of sodium azide in 4.5 ml of water. The temperature was thereupon raised to 18-20° and a white precipitate separated from the solution. The suspension obtained was kept at 5° for 5 min and at room temperature for 30 min and then diluted with 100 ml of cold water and kept at 0° for a further hour. The slightly yellowish precipitate of 2-naphthoazide was collected by filtration, washed with cold water, and dried to constant weight in a desiccator over calcium chloride. The yield was 3.86 g (89%).

2-Naphthylamine hydrochloride. The azide of 2-naphthoic acid (3.86 g) was dissolved with heating in 55 ml of anhydrous alcohol and the solution boiled in a flask with a reflux condenser until the evolution of nitrogen ceased (3 hr) and then for a further 40 min. The light brown solution was filtered to remove the slight precipitate and the alcohol was evaporated. To the light brown crystalline urethan remaining in the flask (4.16 g) was added a solution of 12 g of potassium hydroxide in 5 ml of water and 40 ml of diethylene glycol (b.p. 238-240°) and the mixture heated for 5 hr at a bath temperature of 165-175°. When cool, the reaction mass was diluted with 40 ml of benzene and 160 ml of water. The organic layer was separated and the aqueous one extracted 4 times with benzene (20-ml portions). The benzene solution was dried with anhydrous sodium sulfate and hydrogen

chloride passed in to precipitate a slightly grayish precipitate of 2-naphthylamine hydrochloride. The yield was 2.98 g (85%).

2-Naphthol. A mixture of 1.98 g of 2-naphthylamine hydrochloride and 100 ml of water was heated almost to boiling in a flask with a reflux condenser, dropping funnel, thermometer, and stirrer. The solid dissolved, leaving a small amount of undissolved tar. The solution was cooled to ~ 50° and 3 ml of concentrated sulfuric acid in 40 ml of water was added with stirring. A voluminous white precipitate of 2-naphthylamine sulfate formed. The suspension obtained was cooled to 15° and 4.00 ml of 0.39 N sodium nitrite solution added to it over a period of 25 min. Stirring was continued for a further 20 min and then the slight excess of nitrous acid was destroyed with urea. The red solution of diazo compound was filtered through cotton wool, diluted with 200 ml of water, and heated to boiling over 15 min. The clear solution then became turbid, nitrogen was evolved, and a red-black tar appeared on the surface. Boiling was continued for 5 min; then the solution was cooled and the 2-naphthol, which precipitated as pink scales, extracted with ether (5 portions of 25 ml each). The ether extract was extracted with 10% sodium hydroxide solution (5 portions of 4 ml each), and the alkaline solution treated with charcoal and acidified with concentrated hydrochloric acid to precipitate 2-naphthol. It formed fine, slightly pinkish crystals. The yield was 1.73 g (72.5%) and the m.p. 116.5-119.5°.

For purification the 2-naphthol was dissolved in 20 ml of 5% sodium hydroxide and filtered through activated charcoal (bed 10 mm high and 10 mm in diameter). The 2-naphthol liberated by acidification (1.60 g) had m.p. 118.5-119.7°. According to literature data [31]: m.p. 122-123°.

cis-o-Cyanocinnamic acid. By the procedure which we described previously [21], the 2-naphthol obtained was converted through 1-nitroso-2-naphthol (90% yield) to cis-o-cyanocinnamic acid (51.3% yield). For purification, the acid obtained (0.88 g, m.p. 131-134.5°) was dissolved in 20 ml of 5% sodium carbonate solution, filtered without suction through a bed of activated charcoal (15 mm high and 10 mm in diameter), and reprecipitated by acidification with concentrated hydrochloric acid. This yield 0.77 g of almost colorless cis-o-cyanocinnamic acid with m.p. 134.5-135.5°. According to data in [15]: m.p. 137°.

trans-o-Carbamidocinnamic acid. cis-o-Cyanocinnamic acid (0.77 g) was hydrolyzed to trans-o-carbamidocinnamic acid by the procedure which we described previously [21]. This yielded 0.46 g (53.5%) of colorless needles with m.p. 232-233°.• According to [16], trans-o-carbamidocinnamic acid has m.p. 239°.

A sample of the acid obtained (0.37 g) was diluted with 0.51 g of unlabeled trans-o-carbamidocinnamic acid (m.p. 235.0-235.4°) and the mixture recrystallized from alcohol; this yielded 0.81 g of colorless needles with m.p. 234.0-235.0°.

Found %:•• C 62.4, 63.1. $C_{10}H_9O_3N$. Calculated %: C 62.8.

Radioactivity: 4027, 4022 μC/mole.

trans-o-Aminocinnamic acid. The trans-o-carbamidocinnamic acid was degraded to trans-o-aminocinnamic acid and carbon dioxide by the Hofmann reaction in the apparatus we described previously [21] (the procedure is also described there). Three experiments were carried out and in each of them 250 mg of trans-o-carbamidocinnamic acid was degraded. The carbon dioxide yield (as barium carbonate) was 87, 91, and 96% and the molar radioactivity was 3937, 3894, and 3900 μC/mole, respectively.

trans-o-Aminocinnamic acid was isolated from the solutions from all three experiments in the form of the hydrochloride, the yield of which was 0.49 g (62.5%). For isolation of the free acid, the hydrochloride and filtrate were neutralized with 0.5 N sodium hydroxide solution to litmus. This gave a lemon yellow precipitate of trans-o-aminocinnamic acid. The yield was 0.35 g and the m.p. 155.5-157.5°. According to literature data [16]: m.p. 158°.

Found %: C 65.6. $C_9H_9O_2N$. Calculated %: C 66.2.

•The melting point of trans-o-carbamidocinnamic acid depends strongly on the heating rate and therefore in all cases we introduced the capillary with the substance at 180° and maintained a heating rate of ~ 20°/min.
••Control of completeness of combustion by the Van Slyke method. See [21] for the procedure for determining the radioactivity.

Radioactivity: 235 μC/mole.

After recrystallization from water, found %: C 66.2.

Radioactivity: 225 μC/mole.

Carbostyril. A sample (0.20 g) of trans-o-aminocinnamic acid was heated with 0.25 ml of concentrated hydrochloric acid and 9 ml of water in a flask with a reflux condenser and the solution obtained boiled for 7 hr. The white precipitate which formed when the solution was cooled was collected by filtration, washed with water and dissolved with gentle heating in 8 ml of 7% sodium hydroxide solution.

When carbon dioxide was passed through the alkaline solution, a white precipitate of carbostyril formed. The yield was 0.09 g. After recrystallization from water and drying for 3.5 hr at 100° in vacuum over calcium chloride, the compound had m.p. 192.5-195°. According to [17]: m.p. 196°.

Ultraviolet spectral data:• λ_{max} (in alcohol) 230 mμ (lg ε 4.57), 268.5 mμ (lg ε 3.88), 328-329 mμ (lg ε 3.81). According to data in [32]: λ_{max} (in alcohol) 230 mμ (lg ε 4.57), 269.5 mμ (lg ε 3.87), 329 mμ (lg ε 3.80).

Found %: C 73.9. C_9H_7ON. Calculated %: C 74.4.

Radioactivity: 216 μC/mole.

SUMMARY

1. A method was developed for degrading 2-methylnaphthalene which makes it possible to isolate the carbon atom of position 1 in the form of CO_2.

2. In the isomerization of 1-^{14}C-1-methylnaphthalene at 320° on an aluminosilicate catalyst, the methyl group was transferred mainly (94.5%) to position 2, which indicates the intramolecular nature of the isomerization process and also the difference in the C_1-C_2 and C_2-C_3 bonds in the naphthalene nucleus.

3. A possible mechanism for the intramolecular isomerization of monomethylnaphthalenes is examined.

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DOUBLE DIAZONIUM SALTS OF THALLIUM

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Continuing work on the absorption spectra of double diazonium salts in the region of N ≡ N valence vibrations, we studied the double diazonium salts of thallium with some p-substituted benzene diazonium salts.

Double diazonium salts of thallium were prepared for the first time and investigated by S. S. Nametkin and N. N. Mel'nikov [1] and A. N. Nesmeyanov, K. A. Kocheshkov, and V. A. Klimova [2, 3]. It was established that thallium chloride forms double salts with aryl diazonium chlorides usually in a ratio of 1 : 1 and only in the case of the o-nitrobenzenediazonium salt was the ratio 2 : 1([o-$NO_2C_6H_4N_2Cl]_2TlCl_3$).

In investigating the absorption spectra of the N ≡ N triple bond in the region of 2150-2300 cm^{-1}, we observed that the position of the absorption maximum of the N ≡ N bond depended on the nature of the solvent from which the double salt was recrystallized and sometimes on the synthesis method. A study of the reason for this phenomenon led us to the conclusion that together with the double diazonium salts of thallium trichloride with a 1 : 1 composition, which have been described in the literature [1-3], there exist double salts with a 2 : 1 composition; the infrared spectra of the two types of salts differ in the absorption maximum of the N ≡ N triple bond. This made it possible for us to check the composition and purity of the double salts formed readily and reliably and also to follow their conversions during synthesis or recrystallization.

By using the reliable identification method of infrared spectra, we were able to prepare a series of double diazonium salts of thallium chloride with the composition $[ArN_2Cl]_2TlCl_3$ for the following diazonium compounds: benzenediazonium, p-toluenediazonium, p-chlorobenzenediazonium, p-bromobenzenediazonium, and p-nitrobenzenediazonium (we were unable to prepare a p-carbethoxybenzenediazonium thallium salt with a 2 : 1 composition).

By using the same identification method, we established that under certain conditions there is the possibility of the conversion of salts with a 1 : 1 composition into salts with a 2 : 1 composition and vice versa. These conversions were achieved with three double salts of thallium chloride with benzenediazonium, p-toluenediazonium, and p-chlorobenzenediazonium chlorides. It was established that when these salts with a 1 : 1 composition were precipitated with ether from methanol solutions there was the "elimination" of a thallium chloride molecule and the formation of a salt with a 2 : 1 composition.

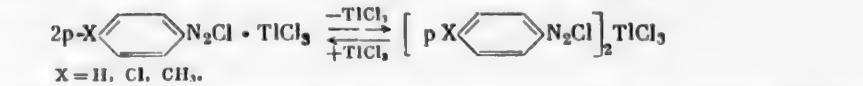
$$2ArN_2Cl \cdot TlCl_3 \rightarrow [ArN_2Cl]_2TlCl_3 + TlCl_3$$

It should be noted that in the case of double salts of thallium trichloride and p-nitrobenzenediazonium chloride, the salts of 1 : 1 and 2 : 1 composition were obtained by different procedures as their conversions did not occur during recrystallization.

The reverse conversion of salts with a 2 : 1 composition to salts with a 1 : 1 composition was accomplished by recrystallization from a mixture of $CH_3OH + H_2O + HCl + TlCl_3$, which makes it possible to regard this conversion as the "addition" of $TlCl_3$.

$$[ArN_2Cl]_2TlCl_3 + TlCl_3 \rightarrow 2ArN_2Cl \cdot TlCl_3$$

Thus, the interaction of these salts may be represented by the following scheme:



X = H, Cl, CH_3.

In the case of the benzenediazonium double salt with a 2 : 1 composition, the conversion to the 1 : 1 salt was incomplete as the salt with a 2 : 1 composition was very unstable and decomposed during the reaction.

It should be noted that all the double salts with a 2 : 1 composition were less stable than salts with a 1 : 1 composition, for example, the salt $[p\text{-}CH_3C_6H_4N_2Cl]_2\ TlCl_3$ decomposed in a few hours to form the salt with a 1 : 1 composition.

Spectra

The table gives the frequencies of the absorption maxima of the N ≡ N bond of the double diazonium salts of thallium chloride in the solid state both for 1 : 1 and 2 : 1 compositions. The $\nu_{N \equiv N}$ frequencies of the corresponding aryl diazonium chlorides are given for comparison.

A peculiarity of the infrared spectra of double diazonium salts of thallium chloride with a 1 : 1 composition in the region of the N ≡ N valence vibrations is the complex nature of the absorption bands. There are either two well-separated bands or more or less clearly expressed asymmetry of the bands, i.e., the presence of an unresolved second maximum. This second maximum of the N ≡ N bond is always considerably weaker in intensity (its frequency is given in brackets in the table). For double salts with a 2 : 1 composition, there is only one symmetrical maximum characterizing the N ≡ N triple bond.

The data presented show that the $\nu_{N \equiv N}$ frequencies of the double salts with a 1 : 1 composition with various substituents in the aromatic ring vary over a range of 43 cm^{-1} (from 2230 to 2273 cm^{-1}) and analogously, the $\nu_{N \equiv N}$ frequencies of the 2 : 1 double salts vary over a range of 46 cm^{-1} (from 2246 to 2292 cm^{-1}). It should also be noted that the frequencies of the maxima $\nu_{N \equiv N}$ for salts with a 1 : 1 composition are lower than the frequencies of salts with a 2 : 1 composition, and while the frequencies of the 1 : 1 double salts are lower than the corresponding diazonium chlorides by 19-30 cm^{-1}, the frequencies of the 2 : 1 salts are less than them by only 5-17 cm^{-1}.

For double diazonium salts with a 1 : 1 composition we obtained a complex spectrum which may indicate additional interaction of the metal atom with the nitrogen of the diazonium group. From this point of view, the disappearance of the second maximum in salts with a 2 : 1 composition might be regarded as a weakening of this interaction; moreover, these salts are closer to aryl diazonium chlorides themselves as regards the position of the absorption maximum.

EXPERIMENTAL

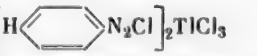
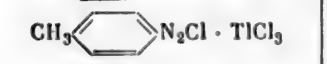
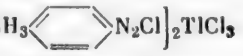
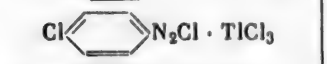
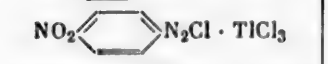
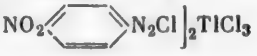
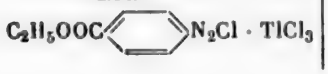
The spectra of the substances were plotted on an IKS-11 single-beam spectrophotometer with a lithium fluoride prism. The samples for spectral measurements were prepared as a suspension of finely ground material in vaseline oil.

The instrument was calibrated with standard spectra of atmospheric moisture, CO_2, and hydrogen chloride vapor.

a) Investigations of Fahr [4] showed that the absorption bands of the triple bond also have a complex structure with aliphatic diazo compounds. He investigated more than 30 diazo ketones and diazo esters, which have two, three, and even four absorption bands in the region of N ≡ N valence oscillations. The appearance of monotypic splitting of the N ≡ N band both for aliphatic diazo compounds of very varied structure and for various double diazonium salts may be regarded as a reflection of structural peculiarities of the molecule itself and not the effect of the crystal lattice.

b) Important results may be given by a study of the absorption spectra of double diazonium salts of thallium chloride in solutions. Preliminary experiments showed that these spectra are complex possibly due to the fact that the choice of an appropriate solvent involves certain difficulties in connection with its effect on the composition of the compound.

N ≡ N Bond Frequency Maxima (in cm^{-1}) for Samples in the Solid State

Compound	Maxima	Diazonium chloride	Maxima	Compound
1 : 1			2 : 1	
	2246 (2257)	2294	2261	
	2233 (2247)	2281	2253	
	2253	2277	2267	
	2230 (2260)	2267	2246	
	2273 (2260)	2303	2292	
	2268	2295	—	—

The benzenediazonium, p-toluenediazonium, p-chlorobenzenediazonium, and p-carbethoxybenzenediazonium double salts with a 1 : 1 composition were prepared according to the published procedure [1-3] with slight changes.

To a cooled (-10 to 0°) solution of aryl diazonium chloride (from 0.02 mole of amine) in dilute hydrochloric acid (1 : 1) was added an acid solution of thallium trichloride (0.025 mole). The precipitate was collected, recrystallized from a mixture of H_2O + CH_3OH + HCl (2 : 1 : 1), washed with dilute hydrochloric acid, and dried in a vacuum desiccator.

$C_6H_5N_2Cl \cdot TlCl_3$ formed a colorless, crystalline precipitate. It had m.p. 73° (decomp.).

Found %: N 6.18, 6.02. $C_6H_5N_2TlCl_4$. Calculated %: N 6.21.

$p\text{-}CH_3C_6H_4N_2Cl \cdot TlCl_3$ formed a colorless crystalline precipitate. It had m.p. 90° (decomp.).

Found %: N 6.10, 6.09. $C_7H_7N_2TlCl_4$. Calculated %: N 6.02

$p\text{-}ClC_6H_4N_2Cl \cdot TlCl_3$ formed a pale yellow crystalline precipitate. It had m.p. 106° (decomp.).

Found %: N 5.92, 6.04. $C_6H_4N_2TlCl_5$. Calculated %: N 5.76

$p\text{-}C_2H_5OOCC_6H_4N_2Cl \cdot TlCl_3$ formed a colorless crystalline precipitate. It had m.p. 92°.

Found %: N 5.43. $C_9H_9N_2O_2TlCl_4$. Calculated %: N 5.35.

The p-bromobenzenediazonium and p-nitrobenzenediazonium double salts were obtained according to the procedure described, with a change in the order of mixing of the component solutions, namely, the thallium trichloride solution was added to the aryl diazonium chloride solution.

$p\text{-}BrC_6H_4N_2Cl \cdot TlCl_3$ formed a pale yellow, crystalline precipitate. It had m.p. 95° (decomp.).

Found %: N 5.39, 5.24. $C_6H_4N_2TlCl_4Br$. Calculated %: N 5.28.

$p\text{-}NO_2C_6H_4N_2Cl \cdot TlCl_3$ formed a yellow, crystalline precipitate. It had m.p. 93° (decomp.).

Found %: N 8.39, 8.44. $C_6H_4N_3O_2TlCl_4$. Calculated %: N 8.46.

The p-bromobenzenediazonium and p-nitrobenzenediazonium double salts with a 2 : 1 composition were obtained by adding a solution of thallium trichloride (0.01 mole) in dilute hydrochloric acid (1 : 1) to a hydrochloric acid solution of aryl diazonium chloride (0.02 mole). The double salt was obtained as a thick oil. The substance was dried in a vacuum desiccator over P_2O_5 and then dissolved in anhydrous alcohol and the solution obtained added to cooled absolute ether. A crystalline precipitate of the double diazonium salt separated.

$[p\text{-}BrC_6H_4N_2Cl]_2TlCl_3$ formed a colorless, crystalline precipitate. It had m.p. 86° (decomp.).

Found %: N 7.37, 7.46. $C_{12}H_8N_4TlCl_5Br_2$. Calculated %: N 7.47.

$[p\text{-}NO_2C_6H_4N_2Cl]_2TlCl_3$ formed a yellow, crystalline precipitate. It had m.p. 58°.

Found %: N 12.50. $C_{12}H_8N_6O_4TlCl_5$. Calculated %: N 12.32.

The benzenediazonium, p-toluenediazonium, and p-chlorobenzenediazonium double salts with a 2 : 1 composition were obtained from the corresponding salts with a 1 : 1 composition in the following way. The double salt with a 1 : 1 composition was dissolved in anhydrous alcohol and the filtered solution added to cooled ether. The precipitate of double salt was collected, washed with dry ether, and dried in a vacuum desiccator.

$[C_6H_5N_2Cl]_2TlCl_3$ formed a finely crystalline, colorless precipitate. It had m.p. 86°.

Found %: N 9.32, 9.46. $C_{12}H_{10}N_4TlCl_5$. Calculated %: N 9.46.

$[p\text{-}CH_3C_6H_4N_2Cl]_2TlCl_3$ formed a colorless, crystalline precipitate. It had m.p. 103° (decomp.).

Found %: N 9.43, 9.28. $C_{14}H_{14}N_4TlCl_5$. Calculated %: N 9.34.

$[p\text{-}ClC_6H_4N_2Cl]_2TlCl_3$ formed a colorless, crystalline precipitate. It had m.p. 117° (decomp.).

Found %: N 8.58, 8.67. $C_{12}H_8N_4TlCl_7$. Calculated %: N 8.48.

Preparation of $C_6H_5N_2Cl \cdot TlCl_3$ from $[C_6H_5N_2Cl]_2TlCl_3$. A sample (0.250 g) of $[C_6H_5N_2Cl]_2TlCl_3$ was dissolved at room temperature in 9 ml of a solution of 0.175 g of $TlCl_3$ in a mixture of $CH_3OH + H_2O + HCl$ (1 : 1 : 1). The solution was filtered and cooled to -15°. The crystalline precipitate was collected, washed with cold, dilute hydrochloric acid, and dried in a desiccator over P_2O_5. We obtained 0.2 g of a colorless precipitate.

Found %: N 7.21, 7.31.

The product obtained was a mixture of unreacted $[C_6H_5N_2Cl]_2TlCl_3$ and $C_6H_5N_2Cl \cdot TlCl_3$.

Preparation of $p\text{-}CH_3C_6H_4N_2Cl \cdot TlCl_3$ from $[p\text{-}CH_3C_6H_4N_2Cl]_2TlCl_3$. Under the conditions of the previous experiment, 1.250 g of $[p\text{-}CH_3C_6H_4N_2Cl]_2TlCl_3$ and 27 ml of a solution of 0.9 g of $TlCl_3$ in a mixture of $CH_3OH + H_2O + HCl$ (1 : 1 : 1) yielded 1.05 g of a colorless, crystalline double salt. It had m.p. 88° (decomp.).

Found %: N 6.18.

Preparation of $p\text{-}ClC_6H_4N_2Cl \cdot TlCl_3$ from $[p\text{-}ClC_6H_4N_2Cl]_2TlCl_3$. Under the conditions of the previous experiment, 1 g of $[p\text{-}ClC_6H_4N_2Cl]_2TlCl_3$ and 20 ml of a solution of 0.5 g of $TlCl_3$ in a mixture of $CH_3OH + H_2O + HCl$ (2 : 2 : 1) yielded 0.75 g of a colorless, crystalline double salt. It had m.p. 104° (decomp.).

Found %: N 6.02.

SUMMARY

1. A series of double diazonium salts of thallium chloride with the composition $[ArN_2Cl]_2TlCl_3$ were prepared.

2. It was established that for double salts with a 2 : 1 composition, the absorption in the region of N ≡ N valence vibrations appears in the form of a symmetrical band, close in position to the corresponding diazonium chlorides, while for salts with a 1 : 1 composition this band has a complex structure.

3. The interconversions of several salts with 2 : 1 and 1 : 1 compositions were accomplished.

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SYNTHESIS AND CONVERSIONS OF SULFIDES OF THE THIOPHENE SERIES

III. PREPARATION AND CLEAVAGE OF SULFOXIDES

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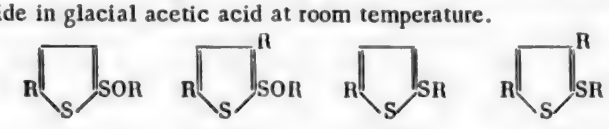
In a previous communication [1] we described a method of blocking the α-position of the thiophene ring, which is suitable for cases where thiophene derivatives are used as intermediates in the synthesis of aliphatic compounds. The essence of this method consists of the replacement of the α-hydrogen by an alkylmercapto group, which can then be removed with Raney nickel, but only together with the ring sulfur. In synthetic problems of another type it is necessary to eliminate the exocyclic sulfur and retain the thiophene ring. This requires a selective agent other than Raney nickel, which breaks all types of C-S bonds. Available literature data on the cleavage of sulfides [2-4] indicate that at the moment there is apparently no satisfactory agent for cleavage of the bond between sulfur and an aromatic ring leading to replacement of an alkylmercapto group by hydrogen. Thus, even after n-butyl phenyl sulfide had been boiled with metallic lithium in ether for 36 hr with subsequent carboxylation, only 11.9% of benzoic acid and 20.5% of thiophenol were formed and 18% of the sulfide was recovered unchanged. This process was even worse with n-butyllithium [3]. When boiled for 12 hr with lithium in dioxane, dibenzothiophan was converted into biphenyl in only 30.5% yield [4].

Sulfoxides are cleaved in the desired direction and in higher yield by the action of n-butyllithium, though in this case many side products are formed, as sulfoxides undergo a variety of conversions under the action of organometallic compounds [5]. In recent years several papers have been published on the cleavage of a bond between carbon in an aromatic ring and an SO group in thianthrene 5-oxide and phenoxathiine 10-oxide [6-8]. In all cases a complex mixture of products from reduction and elimination of sulfoxide groups was obtained. In addition, in one of these papers [7] it was stated that the action of n-butyllithium on diphenyl sulfoxide at -70° and then treatment with carbon dioxide gave a good yield of benzoic acid. The form of the compound in which the sulfur was eliminated was not mentioned in this work; it was only reported that C_4H_9SH was isolated [8].

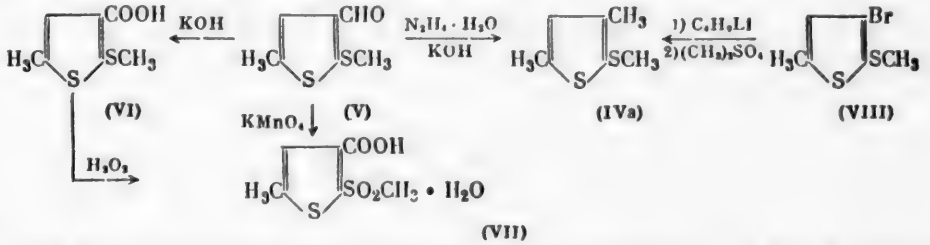
In our first experiments on cleavage of the bond between an alkylmercapto group and a thiophene ring, alkyl thienyl sulfides were treated with lithium. However, it was not possible to obtain 5-ethyl-2-thiophenecarboxylic acid from ethyl 5-ethyl-2-thienyl sulfide by this method. With such sulfides n-butyllithium gives products from substitution of the hydrogen by metal [9]. In connection with this we investigated the reaction of n-butyllithium at a low temperature with alkyl alkylthienyl sulfoxides of types (I) and (II), which were previously unknown. They were obtained in good yield by oxidation of the corresponding sulfides (III) and (IV) with 30% hydrogen peroxide in glacial acetic acid at room temperature.



a) R = CH_3, b) R = C_2H_5.

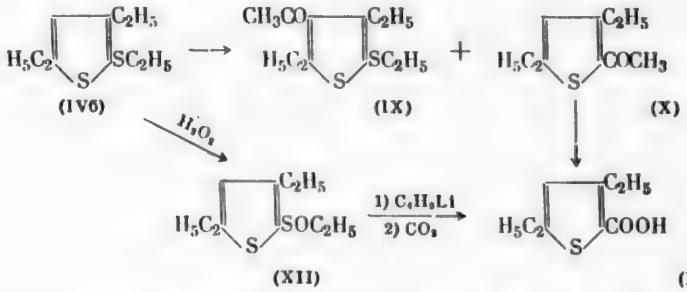
These sulfoxides were mobile oils which were unstable to heat. The sulfoxides (I) distilled in vacuum with resinification, while sulfoxides (II) decomposed during distillation to form the starting sulfides and therefore they were purified by chromatography [10]. Sulfoxides (I) and (II) with R = CH_3 dissolved in water readily while sulfoxides of the same type with R = C_2H_5 were almost insoluble in water. In order to be certain that the structure of these sulfoxides actually corresponded to formulas (I) and (II), we oxidized one of them, methyl 5-methyl-2-thienyl sulfoxide, to the sulfone; the latter was found to be identical to the sulfone obtained by reaction of lithium 5-methyl-2-thienylsulfinate with methyl iodide.

The synthesis of the starting sulfides of type (III) was described previously [1]. We prepared their homologs of type (IV) for the first time by reduction of 2-ethylmercapto-5-ethyl-3-acetothienone [1] and 2-methylmercapto-5-methyl-3-thiophenaldehyde (V) by a modification of the Kizhner method [11]. The aldehyde (V) was obtained in 71% yield from methyl 5-methyl-2-thienyl sulfide by the action of N-methylformanilide in the presence of phosphorus oxychloride. This again confirmed the activating effect of an alkylmercapto group on the thiophene nucleus, as 2,5-dimethylthiophene is only 20-40% formylated [12, 13]. Aldehyde (V) was converted by the Cannizzaro reaction into the previously known 2-methylmercapto-5-methyl-3-thiophenecarboxylic acid (VI), which confirmed its structure; when oxidized with potassium permanganate [14], it gave 2-methylsulfonyl-5-methyl-3-thiophenecarboxylic acid (VII), which crystallized with one molecule of water. This acid was converted into the amide, which did not contain water of crystallization.



The sulfide (IVa) could also be obtained by the action of n-butyllithium and then dimethyl sulfate on 3-bromo-5-methylmercapto-2-methylthiophene (VIII); the latter was formed by bromination of methyl 5-methyl-2-thienyl sulfide with bromide-bromate solution. This again confirms that bromine replaces the β-hydrogen [1]. However, it is considered that under analogous conditions alkyl 3-thienyl sulfides are oxidized to sulfoxides [15]. Under the conditions described in [15], ethyl 5-ethyl-2-thienyl sulfide also gives 3-bromo-5-ethylmercapto-2-methylthiophene, which was obtained previously [1]. We did not observe the formation of sulfoxide in this case.

Acetylation of ethyl 3,5-diethyl-2-thienyl sulfide (IVb, R = C_2H_5) with acetyl chloride, which is the first stage in the preparation of ethyl 3,4,5-triethyl-2-thienyl sulfide, formed a mixture of two ketones, namely, 5-ethylmercapto-2,4-diethyl-3-acetothienone (IX) and 3,5-diethyl-2-acetothienone (X); they could only be characterized in the form of 2,4-dinitrophenylhydrazones.



Due to the low accessibility and difficulty of isolation, ketone (IX) was not reduced. The structure ascribed to ketone (X) was confirmed by oxidation to acid (XI), which was found to be identical with the acid formed as a result of cleavage of ethyl 3,5-diethyl-2-thienyl sulfoxide (XII) (see below).

The conditions for cleaving sulfoxides by n-butyllithium were investigated on the example of ethyl 5-ethyl-2-thienyl sulfoxide (Ib). For convenience, the decomposition product was isolated in the form of the carboxylic acid. The best yield of 5-ethyl-2-thiophenecarboxylic acid was obtained by the action of 2 moles of n-butyllithium at -70° (see table).

Cleavage of Ethyl 5-Ethyl-2-thienyl Sulfoxide

Expt. No.	Amt. of n-C_4H_9Li (in moles)	Temperature	Mixing time (in hr)	Yield of crude 5-ethyl-2-thiophenecarboxylic acid (%)
1	1	—10°	1.5	—
2	2	—10	2.5	43.3
3	1	—70	0.5	24
4	2	—70	0.5	54
5	2	—70	2.5	52.7
6	3	—70	4	50

When cleaved under these conditions, methyl 5-methyl-2-thienyl sulfoxide (Ia), methyl 3,5-dimethyl-2-thienyl sulfoxide (IIa), and ethyl 3,5-diethyl-2-thienyl sulfoxide (IIb) yielded 5-methyl-2-thiophenecarboxylic, 3,5-dimethyl-2-thiophenecarboxylic, and 3,5-diethyl-2-thiophenecarboxylic acids, respectively. The last acid was obtained for the first time. In these cases the sulfoxides were cleaved in low yield. As yet we do not know the reasons for this phenomenon. In addition to the acids mentioned, in each experiment we also isolated a small amount of neutral substances of unknown structure, which gave qualitative reactions [16] with phosphomolybdic acid for sulfides and sulfoxides.

EXPERIMENTAL

2-Methylmercapto-5-methyl-3-thiophenaldehyde (V). Over a period of 40 min, 30 g of methyl 5-methyl-2-thienyl sulfide was added to 32 g of N-methylformanilide and 35.7 g of phosphorus oxychloride at 20-30° and then the reaction mixture was heated at 50-60° for 2 hr and left overnight. The dark brown thick mass was poured into a mixture of 150 g of ice and 80 ml of water and the aqueous layer separated and extracted three times with ether. The ether solution was washed three times with dilute hydrochloric acid (25 g of conc. HCl in 200 ml of water), the aqueous extracts were extracted with ether, and the combined ether extracts washed with sodium bicarbonate solution and water, and dried with magnesium sulfate; the solvent was removed in vacuum and the residue distilled to give 25.5 g of aldehyde (71.2% yield) with b.p. 120-122° at 2 mm. The aldehyde crystallized on prolonged cooling. After recrystallization from ligroin, the aldehyde melted at ~ 20° and had $n^{20}D$ 1.6291.

Found %: C 49.21, 49.25; • H 4.78, 4.81; S 36.79, 36.88. $C_7H_8OS_2$. Calculated %: C 48.80; H 4.68; S 7.23.

After recrystallization from dilute alcohol, heptane, and ligroin, the phenylhydrazone of 2-methylmercapto-5-methyl-3-thiophenaldehyde melted at 69-70.5°.

Found %: N 10.42. 10.46. $C_{13}H_{14}N_2S_2$. Calculated %: N 10.68.

Hydrate of 2-methylsulfonyl-5-methyl-3-thiophenecarboxylic acid (VII). A. A saturated aqueous solution of $KMnO_4$ was gradually added to a mixture of 0.6 g of 2-methylmercapto-5-methyl-3-thiophenaldehyde and 10 ml of water containing 5 drops of 10% NaOH solution until the color no longer disappeared. The mixture formed was acidified with 25% sulfuric acid and treated with sodium bisulfite solution to dissolve the manganese dioxide. The acid (0.4 g) was collected by filtration and recrystallized from benzene and from water; it had m.p. 161° and the neutralization equivalent found was 237.35; calculated 238.28.

B. A mixture of 0.6 g of 2-methylmercapto-5-methyl-3-thiophenecarboxylic acid, 6 ml of acetic acid, and 1.2 g of 30% hydrogen peroxide was heated for 1.5 hr on a water bath. The cooled solution was diluted with water and the precipitate collected, washed with water, and dried (weight 0.6 g). After two recrystallizations from water, the acid melted at 161.5°; a mixture with the acid described in section A had the same melting point.

Found %: C 35.00, 35.23; H 4.22, 4.33; S 26.50, 26.51. $C_7H_8O_4S_2 \cdot H_2O$. Calculated %: C 35.28; H 4.25; S 26.91.

•A similar deviation of the amount of carbon formed from the theoretical value has been reported for aldehydes of the thiophene series [14].

2-Methylsulfonyl-5-methyl-3-thiophenecarbonamide was prepared from 0.18 g of the hydrate of 2-methylsulfonyl-5-methyl-3-thiophenecarboxylic acid by the action of thionyl chloride and then dry ammonia. After two recrystallizations from water, it melted at 190°.

Found %: C 38.09, 38.20; H 4.35, 4.21; S 28.97, 28.86; N 6.52, 6.58. $C_7H_9O_3NS_2$. Calculated %: C 38.35; H 4.14; S 29.25; N 6.39.

2-Methylmercapto-5-methyl-3-thiophenecarboxylic acid (VI). A solution of 1.1 g of 2-methylmercapto-5-methyl-3-thiophenaldehyde in 11 ml of 25% methanolic KOH was left for 12 hr at room temperature, then boiled for 1 hr, cooled, diluted with water, and extracted with ether. The aqueous solution was concentrated in vacuum and acidified with hydrochloric acid. The acid liberated was collected by filtration (0.36 g) and recrystallized from benzene and dilute alcohol, when it had m.p. 193-193.5°. A mixed melting point of this acid with 2-methylmercapto-5-methyl-3-thiophenecarboxylic acid obtained by oxidation of 2-methylmercapto-5-methyl-3-acetylthiophene [1], was not depressed.

Methyl 3,5-dimethyl-2-thienyl sulfide (IVa). A. By reduction of 2-methylmercapto-5-methylthiophenaldehyde. A mixture of 20.3 g of aldehyde, 17.4 g of hydrazine hydrate, and 150 ml of diethylene glycol was boiled for 30 min, cooled to 70°, and diluted with a solution of 20 g of KOH in the minimum amount of water, and boiling continued for a further hour. The sulfide and excess hydrazine hydrate were then removed by steam distillation and the residue boiled at 200° until the evolution of nitrogen ceased. The distillate was extracted with ether. The ether solution was washed with dilute hydrochloric acid, sodium bicarbonate solution, and water and dried with magnesium sulfate. Vacuum distillation yielded 11.0 g of sulfide with b.p. 98° at 14 mm and $n^{20}D$ 1.5662. The residue from the distillation was diluted with an equal volume of water and treated analogously to yield 3.3 g of sulfide. The total yield was 78%.

Found %: C 53.06, 53.17; H 6.52, 6.55; S 39.84, 39.90. $C_7H_{10}S_2$. Calculated %: C 53.11; H 6.37; S 40.52.

B. Through 3-bromo-5-methylmercapto-2-methylthiophene. Over a period of 1.5 hr, 110 ml of an aqueous bromide-bromate solution with a bromine concentration of 64 g/liter was added with stirring to a mixture of 6 g of methyl 5-methyl-2-thienyl sulfide, 50 ml of ether, and 15 ml of concentrated hydrochloric acid at 10-15°. After 15 min the ether layer was separated and the aqueous layer extracted with ether. The ether extracts were washed with 10% NaOH solution and water and dried with magnesium sulfate. Vacuum distillation yielded 6.9 g of 3-bromo-5-methylmercapto-3-methylthiophene with b.p. 86-87° at 2 mm (75% yield). To a solution of this bromide in 70 ml of dry ether at -10° was added 20 ml of an ether solution of n-butyllithium. After the mixture had been stirred for an hour at 0°, 4.7 g of dimethyl sulfate was gradually added. The mixture was stirred for 6 hr and left overnight. On the following day, 50 ml of water was added, the ether layer separated, and the aqueous layer extracted 3 times with ether. The ether extract was washed 3 times with dilute ammonia solution and water and dried with magnesium sulfate. Vacuum distillation gave 2.3 g (42% yield) of sulfide with b.p. 91-95° at 10 mm and $n^{20}D$ 1.5604. After redistillation, the substance had b.p. 94-96° at 16 mm and $n^{20}D$ 1.5665.

Bromination of ethyl 5-ethyl-2-thienyl sulfide under the conditions of Houff and Schuetz [15]. A solution of 4 g of sulfide and 7 ml of concentrated hydrochloric acid in 120 ml of glacial acetic acid was stirred while 58 ml of bromide-bromate solution (containing 64 g/liter of bromine) was gradually added and then the mixture was heated at 45° for 5 min. The liberated oil was separated and the acetic acid solution evaporated in vacuum. The residue was diluted with water, neutralized with 10% NaOH, and extracted with ether. The ether solution was combined with the oil, washed with 10% NaOH and water, and dried with magnesium sulfate. Removal of the ether left 3.5 g of oil (60% yield), which contained bromine but no sulfoxide group (reaction with phosphomolybdic acid). After one distillation in vacuum, the 3-bromo-5-ethylmercapto-2-ethylthiophene [1] had b.p. 124° at 5 mm and $n^{20}D$ 1.5885. By the action of n-butyllithium and carbon dioxide, the bromide was converted to 2-ethylmercapto-5-ethyl-3-thiophenecarboxylic acid, which melted at 126° after recrystallization from 50% alcohol. A mixed melting point with the acid prepared previously [1] was not depressed.

Ethyl 3,5-diethyl-2-thienyl sulfide (IVb). As described for methyl 3,5-dimethyl-2-thienyl sulfide, from 45.[illegible] g of 2-ethylmercapto-5-ethyl-3-acetothienone, 31.8 g of hydrazine hydrate, 35.7 g of potassium hydroxide, and 280 ml of diethylene glycol we obtained 22.5 g (53% yield) of ethyl 3,5-diethyl-2-thienyl sulfide with b.p. 123-123.5° at 10 mm and $n^{20}D$ 1.5445.

Found %: C 59.90, 59.86; H 7.87, 7.98; S 31.65, 31.86. $C_{10}H_{16}S_2$. Calculated %: C 59.94; H 8.04; S 32.02.

Acetylation of ethyl 3,5-diethyl-2-thienyl sulfide. To a mixture of 10 g of sulfide and 4.3 g of acetyl chloride in 150 ml of dry benzene at 0-2° was gradually added 13 g of stannic chloride in 15 ml of dry benzene. After being stirred at room temperature for 2 hr, the dark solution was treated with 30 ml of dilute hydrochloric acid (1 : 10). The benzene layer was separated and the aqueous one extracted with ether. The benzene-ether extract was washed with water and dried with magnesium sulfate. The solvent was removed in vacuum and the residual oil was decolorized by heating with water and extracted with ether. The ether solution was dried with magnesium sulfate. The residue after removal of the ether was distilled. We obtained fractions: 1st, b.p. 100-114° at 3 mm, 4.5 g, $n^{20}D$ 1.5446; 2nd, b.p. 125-135° at 4 mm, 2.2 g, $n^{20}D$ 1.5575; 3rd, b.p. 165-172° at 4 mm, 0.4 g, $n^{20}D$ 1.5658.

Repeated vacuum distillations of the 1st fraction yielded a substance with b.p. 111-111.5° at 5 mm. A 2,4-dinitrophenylhydrazone was prepared from it and after recrystallization from acetic acid and from alcohol, this melted at 155-155.5° and corresponded in composition to the hydrazone of 3,5-diethyl-2-acetothienone.

Found %: C 52.86, 52.87; H 4.98, 5.09; N 15.34, 15.20; S 8.73, 8.80. $C_6H_{18}O_4N_4S$. Calculated %: C 52.73; H 4.98; N 15.37; S 8.79.

Two distillations of the 2nd fraction yielded a ketone with b.p. 124.5° at 2 mm. After two recrystallizations from alcohol, the 2,4-dinitrophenylhydrazone of this ketone melted at 89-90° and corresponded in composition to the hydrazone of 5-ethylmercapto-2,4-diethyl-3-acetothienone.

Found %: C 51.24, 51.36; H 5.29, 5.30; N 13.25, 12.98. $C_{18}H_{22}O_4N_4S_2$. Calculated %: C 51.16; H 5.25; N 13.26.

In an attempt to oxidize 1.3 g of this ketone to the corresponding acid, it was not possible to isolate a crystalline compound.

3,5-Diethyl-2-thiophenecarboxylic acid (XI). To 2.2 g of 3,5-diethyl-2-acetothienone in 15 ml of dry pyridine was added 3.1 g of iodine. The mixture was heated on a water bath for 40 min and left overnight. On the following day the pyridine was removed in vacuum and the residue boiled for 1 hr with 1.5 g of NaOH in 75 ml of 50% alcohol. The cooled solution was diluted with an equal volume of water and acidified with 10% hydrochloric acid. The liberated oil was extracted with ether and the ether solution washed with sodium hyposulfite solution and water and dried with magnesium sulfate. Removal of the ether left a dark crystalline substance, which was purified by reprecipitation from an alkaline solution. We obtained 0.35 g of acid with m.p. ~81°. After two recrystallizations from dilute alcohol, the acid melted at 85-85.5°.

Found %: C 58.87, 58.92; H 6.67, 6.90; S 17.24, 17.19. $C_9H_{12}O_2S$. Calculated %: C 58.67; H 6.57; S 17.40.

Ethyl 5-ethyl-2-thienyl sulfoxide (Ib). To a solution of 10.4 g of ethyl 5-ethyl-2-thienyl sulfide in 60 ml of glacial acetic acid was added 7.6 g of 29% of hydrogen peroxide with cooling so that the temperature of the mixture did not rise above 40°. After the mixture had been kept at room temperature for 3 days, the acetic acid was removed in vacuum and the residual oil dissolved in ether. The ether solution was washed with sodium bicarbonate solution and water and dried with magnesium sulfate. Removal of the ether left 8.9 g (78% yield) of crude sulfoxide with $n^{20}D$ 1.5623, which distilled in vacuum with resinification and then had b.p. 134-135° at 2 mm and $n^{20}D$ 1.5638.

Found %: C 51.04, 50.80; H 6.48, 6.44; S 33.76, 33.76. $C_8H_{12}OS_2$. Calculated %: C 51.02; H 6.42; S 34.06.

In some experiments the yield of crude sulfoxide reached 90%. The oxidation gave a lower yield in acetone.

Ethyl 3,5-diethyl-2-thienyl sulfoxide (IIb). As described in the previous experiment, from 9 g of ethyl 3,5-diethyl-2-thienyl sulfide we obtained 8.5 g of sulfoxide as a light oil with $n^{20}D$ 1.5510. When vacuum distilled, the sulfoxide resinified strongly and was partly converted into the original sulfide with b.p. 87° at 2 mm and $n^{20}D$ 1.5440.

Found %: C 60.26; H 8.22; S 31.50. $C_{10}H_{16}S_2$. Calculated %: C 59.94; H 8.04; S 32.02.

A solution of 1 g of the crude sulfoxide in dry benzene was partially decolorized by means of charcoal and purified by chromatography on KSM grade silica gel. Dry ethyl acetate was used for elution and the first,

colored portion of the eluate was discarded. The ethyl acetate was removed in vacuum and the residue dried in vacuum, when it had $n^{20}D$ 1.5539.

Found %: C 55.39, 55.37; H 7.50, 7.44; S 29.22, 29.27. $C_{10}H_{16}OS_2$. Calculated %: C 55.51; H 7.45; S 29.64.

Methyl 5-methyl-2-thienyl sulfoxide (Ia). Methyl 5-methyl-2-thienyl sulfide (13.1 g) was oxidized with hydrogen peroxide in acetic acid as described above. The acetic acid was removed in vacuum. The remainder of it was removed by three distillations with water and alcohol. The sulfoxide was dissolved in ether and treated with manganese dioxide to decompose H_2O_2. The ether solution was dried with magnesium sulfate. The oil remaining after removal of the ether distilled at 177-120° (1 mm). We obtained 10.5 g (72% yield) of sulfoxide with $n^{20}D$ 1.5852. In contrast to ethyl 5-ethyl-2-thienyl sulfoxide, this substance dissolved in water.

Found %: C 44.72, 44.75; H 4.97, 5.16; S 39.78, 39.58. $C_6H_8OS_2$. Calculated %: C 44.96; H 5.03; S 40.02.

Methyl 3,5-dimethyl-2-thienyl sulfoxide (IIa). This compound was obtained as described in the previous experiment. It resinified strongly during vacuum distillation and therefore the crude product with $n^{20}D$ 1.5600 was used for further work.

Ethyl 5-ethyl-2-thienyl sulfone. A mixture of 2 g of ethyl 5-ethyl-2-thienyl sulfide, 4 ml of 27% hydrogen peroxide (50% excess), and 20 ml of glacial acetic acid was heated on a water bath for 1.5 hr. The mixture was poured onto ice, neutralized with 20% NaOH solution, and extracted with ether. The ether solution was dried with magnesium sulfate, the ether removed, and the residue vacuum distilled. We obtained 1.2 g of sulfone with b.p. 145° at 4 mm and $n^{20}D$ 1.5393.

Found %: C 47.12, 47.04; H 5.91, 5.96; S 30.98, 30.67. $C_8H_{12}O_2S_2$. Calculated %: C 47.03; H 5.92; S 31.39.

Methyl 5-methyl-2-thienyl sulfone. a) A mixture of 2 g of methyl 5-methyl-2-thienyl sulfoxide and 2 ml of 29% hydrogen peroxide in 20 ml of glacial acetic acid was heated for 45 min on a water bath. The solution was poured onto ice and neutralized with 20% sodium hydroxide. The precipitated oil crystallized on cooling. After recrystallization from heptane and from ligroin, the sulfone (1.7 g) melted at 40°.

Found %: C 41.17, 41.12; H 4.63, 4.53; S 35.89, 36.06. $C_6H_8O_2S_2$. Calculated %: C 40.88; H 4.57; S 36.39.

b) A solution of 10 g of sulfur dioxide in 50 ml of dry ether was gradually added at -50° to 5-methyl-2-thienyllithium obtained by boiling an ether solution of 10 g of 2-methylthiophene and an equivalent amount of n-butyllithium for 40 min. The precipitate was collected, washed with dry ether, and dried in vacuum. The yield was quantitative. A mixture of 3 g of lithium 5-methyl-2-thienylsulfinate and 10 g of methyl iodide in 45 ml of 50% alcohol was boiled for 13 hr. The excess methyl iodide and alcohol were removed in vacuum. The oil liberated was extracted with ether and the ether solution washed with water and dried with magnesium sulfate. Removal of the solvent left 2 g (63.5% yield) of a crystalline substance. After two recrystallizations from heptane, the sulfone melted at 40°. A mixed melting point with the sulfone obtained by oxidation of the sulfoxide was not depressed.

Cleavage of sulfoxides. a) To a solution of 4 g of ethyl 5-ethyl-2-thienyl sulfoxide in 40 ml of dry ether at -70° was gradually added 35 ml of an ether solution of n-butyllithium. When the first drops of butyllithium were added, a white precipitate formed and this completely dissolved when 1 equiv. of butyllithium had been added. The solution was then stirred for 30 min at -70° and poured into a mixture of dry ice and ether. After treatment with water, the ether layer was separated, washed with water, and dried with magnesium sulfate. From the ether solution we isolated 0.5 g of oil, which gave a positive reaction for sulfide with phosphomolybdic acid. The ether was removed from the aqueous layer and the solution acidified with dilute hydrochloric acid (1 : 1) with cooling. The precipitated acid (1.8 g, 54% yield) melted at 65°. After recrystallization from water and from heptane, the substance had m.p. 70° (according to data in [17]: m.p. 71°). A mixed melting point with an authentic sample of 5-ethyl-2-thiophenecarboxylic acid was not depressed.

Found %: C 53.64, 53.53; H 5.02, 4.96; S 20.41, 20.34. $C_7H_8O_2S$. Calculated %: C 53.82; H 5.16; S 20.53.

b) In the same way, from 3 g of ethyl 3,5-diethyl-2-thienyl sulfoxide we obtained 0.6 g (24%) of crude 3,5-diethyl-2-thiophenecarboxylic acid with m.p. ~ 80°, which melted at 84.5-85° after two recrystallizations from dilute alcohol. A mixed melting point with the acid obtained by oxidation of 3,5-diethyl-2-acetothienone was not depressed.

Found %: C 58.73, 58.77; H 6.62, 6.61; S 17.49, 17.45. $C_9H_{12}O_2S$. Calculated %: C 58.67; H 6.57; S 17.40.

c) By the method described, from 3.2 g of methyl 5-methyl-2-thienyl sulfoxide we obtained 0.7 g (24.7%) of 5-methyl-2-thiophenecarboxylic acid, which melted at 138° after recrystallization from water and from heptane. A mixed melting point with an authentic sample of 5-methyl-2-thiophenecarboxylic acid was not depressed. According to data in [18]: m.p. 138-138.5°.

d) From 2.5 g of methyl 3,5-dimethyl-2-thienyl sulfoxide we obtained 0.3 g (13.5%) of 3,5-dimethyl-2-thiophenecarboxylic acid, which was recrystallized from heptane and dilute alcohol, when it melted at 171.5-172.5° (according to data in [19]: m.p. 171-172°).

Found %: C 53.67, 53.83; H 5.18, 5.20; S 20.44, 20.44. $C_7H_8O_2S$. Calculated %: C 53.82; H 5.16; S 20.53.

An amide was prepared from the acid and after recrystallization from water and from heptane it melted at 115-116° (according to data in [19]: m.p. 115-116°).

Found %: N 8.73, 8.74. C_7H_9ONS. Calculated %: N 9.02.

SUMMARY

1. The action of n-butyllithium on alkyl alkylthienyl sulfoxides eliminated the exocyclic sulfur atom while the thiophene ring remained intact.

2. The preparation of a series of alkyl alkylthienyl sulfoxides from the corresponding sulfides is described.

3. 3-Formyl and 3-acetyl derivatives of alkyl 5-alkyl-2-thienyl sulfides are readily reduced to the corresponding alkyl derivatives by the Huang-Minlon modification of the Kizhner method.

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SYNTHESIS OF 2-SUBSTITUTED 4-PENTAMETHYLENE-5,6-TETRAMETHYLENE-2,3,4,5-TETRAHYDROPYRIMIDINES

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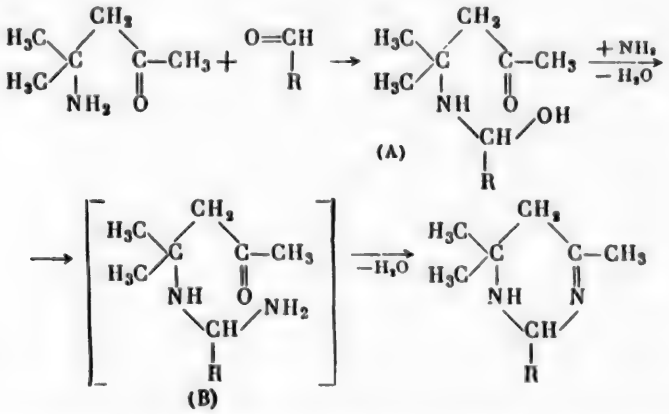
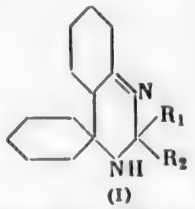
In our previous work [1], the condensation of cyclohexanone with ammonia was used to synthesize 2,4-dipentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidine (Ia), which readily underwent acid hydrolysis to form the β-amino ketone 2-(1-aminocyclohexyl)-cyclohexanone (II).

In the preparation of 2,2,4,4,6-pentamethyl-2,3,4,5-tetrahydropyrimidine ("acetonine") from acetone and ammonia, Bradbury and his co-workers [2] suggested that the intermediate product in this reaction is diacetoneamine. Asinger and his co-workers [3] carried out reactions of some β-amino ketones with ammonia and carbonyl compounds. This yielded various substituted tetrahydropyrimidines. The hypothesis was put forward [4] that such reactions are possible due to the formation of the very reactive intermediate amino hydroxy compound, which is formed as a result of addition of ammonia at the carbonyl group. In some other work [3], Asinger and his co-workers proposed a different mechanism for the synthesis of tetrahydropyrimidines from β-amino ketones, ammonia, and carbonyl compounds. On the basisof an investigation [5] of the Mannich reaction, they proposed that at first the β-amino ketone adds to the > C = O group of the third component with the formation of an N-semiacetal (A), the hydroxyl group of which reacts with ammonia. By the elimination of water, the N,N-acetal thus obtained (B) is readily converted into the corresponding substituted tetrahydropyrimidine according to the following scheme:



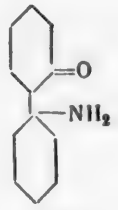
The mechanism of formation of β-amino ketones in the preparation of compounds (I) from ketones and ammonia has not been discussed in the literature. However, in analogy with the well-known Mannich reaction [6], according to which it is also possible to obtain a β-amino ketone from two carbonyl compounds and an amine, the formation of β-amino ketones in the synthesis of substituted tetrahydropyrimidines may be explained by the intermediate formation of either a hydroxy ketone, as an aldol condensation product, or the product of addition of the amine to the carbonyl group.

In the present work it was shown that (Ia) is formed not only from cyclohexanone and ammonia, but also by condensation of (II) with cyclohexanone and ammonia compound (II) and NH_3 also react with other carbonyl compounds to form substituted tetrahydropyrimidines. By using acetone, methyl ethyl ketone, or acetaldehyde as the third component, it was possible to obtain previously undescribed tetrahydropyrimidines (Ib, Ic, and Id).



(I)

(Ia) R_1 $R_2 = (CH_2)_5$; (Ib) $R_1 = R_2 = CH_3$; (Ic) $R_1 = CH_3$, $R_2 = C_2H_5$; (Id) $R_1 = H$, $R_2 = CH_3$.



(II)

In order to study the mechanism of formation of (I) and (II), we prepared the addition product of ammonia and cyclohexanone in a molar ratio of 1 : 1 and this was found to be stable at a temperature below -80°. It reacted neither with cyclohexanone nor (II) either in the presence of ammonium chloride or in its absence. Hence, it follows that contrary to hypotheses in the literature [4], this product from the reaction of cyclohexanone and ammonia is not the intermediate product in the formation of (II) or in the condensation of the latter with cyclohexanone and ammonia. Therefore, the more probable intermediate product in the formation of (II) is the hydroxy ketone. In the preparation of (I) from (II), carbonyl compounds, and ammonia, one must give preference to the reaction mechanism based on the intermediate formation of the N-semiacetal (A, and the N,N-acetal (B) [3].

The (II) required in the present work was obtained in quantitative yield by hydrolysis of (Ia), which is more convenient than the reduction of cyclohexanone by the Meerwein-Ponndorf reaction in the presence of ammonia in 40% yield [7].

EXPERIMENTAL

2-(1-Aminocyclohexyl)-cyclohexanone (II). A mixture of 500 ml of water, 110 ml of concentrated hydrochloric acid, and 137 g of (Ia) was left to stand for 12 hr. After extraction of the hydrolysis solution with benzene (5 × 75 ml) and ether (100 ml), ammonia was passed into this solution to an alkaline reaction. The (II) precipitated was extracted with ether (2 × 150 ml). The ether solution was dried with calcium chloride and filtered. The bulk of the ether was removed on a water bath at 50°. Removal of the ether residues in vacuum yielded 90 g of (II) (92%), which was identical with that isolated previously [1].

2,4-Dipentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidine (Ia). Ammonia was passed into a mixture of 50 g of (II), 25 g of cyclohexanone, 3 g of $CaCl_2$, and 1.5 g of NH_4Cl for 7 hr with stirring and cooling with water. Washing and drying yielded 65 g (93%) of (Ia) with m.p. 52°, which did not depress the melting point of (Ia) synthesized from cyclohexanone and ammonia [1].

2,2-Dimethyl-4-pentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidine (Ib). Ammonia was passed for 9 hr into a mixture of 50 g of (II), 16 g of acetone, 3 g of $CaCl_2$, 1.5 g of NH_4Cl, and 70 ml of methanol, which was stirred and cooled with water. After the layers had separated, the lower layer was dissolved in 350 ml of ether. The ether solution was filtered and the bulk of the ether removed on a water bath at 50°. Removal of the ether residues in vacuum yielded 54.6 g (91%) of (Ib) as a viscous, slightly yellowish liquid, which was soluble in many organic solvents, but insoluble in water. (Ib) was hydrolyzed readily by acids, even in the cold, was resistant to alkalis at normal temperature, and not very stable in air.

d^{20}_4 1.002, $n^{20}D$ 1.5128, MR_D 70.16; calc. 70.21.

Found %: C 77.02, 77.22; H 11.12, 11.23. Equiv. 118. $C_{15}H_{26}N_2$. calculated %: C 76.96; H 11.10. Equiv. 117.

2-Methyl-2-ethyl-4-pentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidine (Ic). Ammonia was passed for 14 hr into a mixture of 63.8 g of (II), 24 g of methyl ethyl ketone, 4 g of $CaCl_2$, 2 g of NH_4Cl, and 70 ml of methanol, which was stirred and cooled with water. After the layers had separated, the lower layer

was treated in the same way as in the previous case. We obtained 77.2 g (90.5%) of (Ic) in the form of a viscous slightly yellowish liquid with properties analogous to (Ib).

d^{20}_4 1.001, $n^{20}D$ 1.5138, MR_D 74.60; calc. 74.83.

Found %: C 77.39, 77.26; H 11.27, 11.28. Equiv. 126. $C_{16}H_{28}N_2$. Calculated %: C 77.44; H 11.28. Equiv. 124.

2-Methyl-4-pentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidine (Id). Ammonia was passed for 1 hr into a mixture of 12.8 g of (II), 0.8 g of $CaCl_2$, 0.4 g of NH_4Cl, and 7 ml of methanol, which was stirred and cooled with water. Then a solution of 2.9 g of acetaldehyde in 7 ml of methanol was gradually added and ammonia again passed for 7 hr. After the layers had separated, the lower layer was treated as indicated above. We obtained 12.5 g (91%) of (Id) in the form of a viscous, yellowish liquid with properties analogous to (Ib).

d^{20}_4 1.02, $n^{20}D$ 1.5202, MR_D 65.5; calc. 65.59.

Found %: C 76.12, 76.23; H 10.82, 10.78. Equiv. 112. $C_{14}H_{24}N_2$. Calculated %: C 76.40; H 10.90. Equiv. 110.

Preparation of the product from the reaction of cyclohexanone and ammonia at low temperature. Into a mixture of 50 ml of benzene and 10 g of cyclohexanone at -15° was passed ammonia for 30 min. The voluminous solid white product which separated was collected by filtration with cooling and washed preliminarily with cold ether. Part of the product was rapidly transferred to a tube, which was then heated to 50°. The ammonia liberated was absorbed in 0.1 N HCl solution. We found 0.0946 g of ammonia. In the tube remained 0.545 g of cyclohexanone with $n^{20}D$ 1.4500; oxime m.p. 88°. The product was readily soluble in methanol, sparingly soluble in benzene and ether, and began to dissociate to ammonia and cyclohexanone when heated to -8 to -7°.

SUMMARY

1. Condensation of 2-(1-aminocyclohexyl)-cyclohexanone (II) with carbonyl compounds and ammonia yielded three new 2-substituted 4-pentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidines (I).

2. It was shown that ammonia readily adds to cyclohexanone to form a compound in a molar ratio of 1 : 1, which is stable at low temperature, and that this compound is not an intermediate product in the preparation of 2-(1-aminocyclohexyl)-cyclohexyl)-cyclohexanone (II) and 2,4-dipentamethylene-5,6-tetramethylene-2,3,4,5-tetrahydropyrimidine (Ia) from cyclohexanone and ammonia.

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CONDENSATION OF UNSATURATED CARBONYL COMPOUNDS AND β-HALO KETONES WITH DERIVATIVES OF β-AMINOETHYL MERCAPTAN AND ETHYLENE DIAMINE. II

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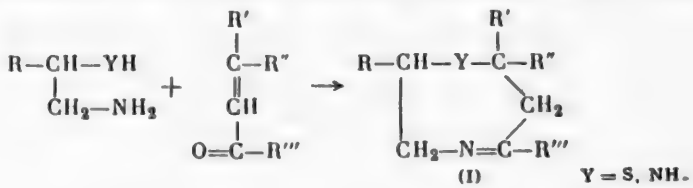
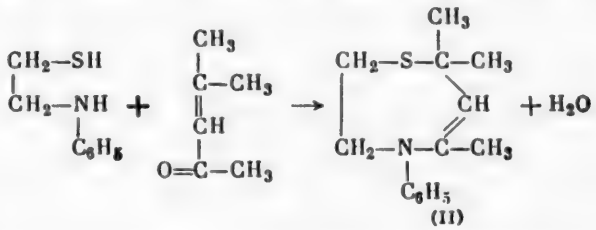
In the first communication [1] we showed that the condensation of β-aminoethyl mercaptan with mesityl oxide and also with methyl β-bromoisobutyl ketone forms a seven-membered heterocycle, namely, 5,7,7-trimethyltetrahydrohepta-1,4-thiazine. In the present work we describe syntheses of new seven-membered heterocyclic bases by condensation of 1,2-amino thiols and 1,2-diamines with α,β-unsaturated ketones.



(I) Y = S, NH.

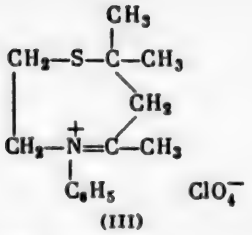
As amino thiols for the condensation we used β-aminoethyl mercaptan and 2-mercaptopropylamine. These amino mercaptans condensed with mesityl oxide and 3-methylhepten-3-one-5. The formation of seven-membered heterocycles proceeded readily with heat evolution by the reaction mixture. Heating on a water bath was sufficient for completion of the reaction. The bases (I) obtained, namely, 2,5,7,7-tetramethyltetrahydrohepta-1,4-thiazine (Y = S, R = R' = R" = R"' = CH_3) and 7-methyl-5,7-diethyltetrahydrohepta-1,4-thiazine (Y = S, R = H, R' = CH_3, R" = R"' = C_2H_5) were converted into the corresponding picrates, perchlorates, and iodomethylates.

We then studied the condensation of β-phenylaminoethyl mercaptan with mesityl oxide. This reaction proceeded less vigorously and its completion required prolonged heating on a water bath (10 hr).



(II)

5,7,7-trimethyl-4-phenyltetrahydrohepta-1,4-triazine (II) decomposed during vacuum distillation. The base was therefore purified by conversion to its quaternary salt (III) by the action of perchloric acid.



(III)

By the action of alkali on the recrystallized quaternary salt (III) it was possible to isolate the pure base (II). An analogous quaternary salt was obtained directly by condensation of β -phenylaminoethyl mercaptan with methyl β -bromoisobutyl ketone.

The seven-membered bases, quaternary salts, and hydrogen halides obtained had active methyl and methylene groups in position 5. Through these groups they readily condensed with aromatic aldehydes and orthoformic ester to form styrils and trimethyne cyanines.

It also seemed interesting to study the properties of seven-membered bases with two nitrogen atoms in the ring. The first such heterocycle was obtained in 1894 by Guareschi [2] in studying the condensation of phorone and mesityl oxide with ethylene diamine. The author showed that in the presence of ethylene diamine, phorone readily decomposes to acetone and mesityl oxide. With ethylene diamine, the latter forms 5,7,7-trimethyltetrahydrohepta-1,4-diazine. An identical base was obtained directly from mesityl oxide and ethylene diamine.

The abstract of this work [2], which was published in an inaccessible journal, did not give the reaction conditions or the constants of the base and its derivatives, apart from the melting point of the platinosulfocyanate. We repeated this synthesis and also obtained the new base 7-methyl-5,7-diethyltetrahydrohepta-1,4-diazine (I, Y = NH, R = H, R' = CH_3, R" = R"' = C_2H_5) by condensation of ethylenediamine with 3-methylhepten-3-one-5. The condensation of ethylene diamine with the unsaturated ketones proceeded readily with heat evolution by the reaction mixture. The yield of bases was 56-60%. The reaction of equimolecular amounts of picric and perchloric acids with the heptadiazine bases yielded the corresponding salts at the tertiary carbon atom, namely, the monopicrates and the monoperchlorates. Alkylation with methyl and ethyl iodides formed quaternary salts. The perchlorates and iodoalkylates obtained from the above bases had active methyl groups in position 5, like the salts of the heptathiazine derivatives.

EXPERIMENTAL

2,5,7,7-Tetramethyltetrahydrohepta-1,4-thiazine. The 2-mercaptopropylamine required for condensation with mesityl oxide was obtained in the following way. 2-Bromopropylamine hydrobromide, obtained from allylamine [3], was mixed with a freshly prepared solution of potassium hydrosulfide in alcohol. The precipitate of potassium bromide was removed and the excess potassium hydrosulfide precipitated with a stream of carbon dioxide. The alcohol was then evaporated to a volume of 150-200 ml. The yield of 2-mercaptopropylamine was determined by titration with iodine. From 20 g of allylamine we obtained 22 g (70%) of 2-mercaptopropylamine.

When an alcohol solution of 22 g (0.24 mole) of 2-mercaptopropylamine was mixed with 23.5 g (0.24 mole) of mesityl oxide, heat was evolved. The mixture was left at room temperature for 10-12 hr. The reaction product was washed with water, the base extracted with ether and dried with sodium sulfate, the ether removed, and the base vacuum distilled. We collected a fraction with b.p. 96-97° (10 mm), which was pure 2,5,7,7-tetramethyltetrahydrohepta-1,4-thiazine. The yield was 21.0 g (41%) and the product had d^{20}_4 0.9837, $n^{21}D$ 1.4970.

Found %: S 18.58, 18.64. $C_9H_{17}NS$. Calculated %: S 18.72.

Mixing alcohol solutions of 0.2 g of 2,5,7,7-tetramethyltetrahydrohepta-1,4-thiazine and 0.27 g of picric acid formed a picrate as yellow crystals. Recrystallization from alcohol yielded 0.25 g (53%) of picrate with m.p. 159-160°.

Found %: N 13.91, 13.96. $C_{15}H_{20}O_7N_4S$. Calculated %: N 13.99.

With stirring and cooling, perchloric acid was added dropwise to an ether solution of 0.5 g of 2,5,7,7-tetramethyltetrahydrohepta-1,4-thiazine to a neutral reaction. A white mass precipitated. Recrystallization from alcohol yielded 0.54 g (68%) of the perchlorate in the form of large lustrous needles with m.p. 195°.

Found %: N 5.04, 5.09; S 11.70; Cl 13.15. $C_9H_{18}O_4NSCl$. Calculated %: N 5.15; S 11.80; Cl 13.05.

7-Methyl-5,7-diethyltetrahydrohepta-1,4-thiazine. A mixture of 10.0 g (0.13 mole) of β-aminoethyl mercaptan and 16.4 g (0.13 mole) of 3-methylhepten-3-one-5 was heated in a sealed tube on a boiling water bath for 5 hr. The reaction product was then dissolved in ether, washed with water, and dried with sodium sulfate. After removal of the ether, the residue was vacuum distilled. The fraction collected at 89-90° (3 mm) was pure base. The yield was 20.5 g (83%) and the product had d^{18}_4 0.9870, $n^{18}D$ 1.5008.

Found %: S 17.34, 17.43. $C_{10}H_{19}NS$. Calculated %: S 17.30.

Mixing alcohol solutions of 0.5 g of 7-methyl-5,7-diethyltetrahydro hepta-1,4-thiazine and 0.65 g of picric acid formed the picrate. Recrystallization from alcohol yielded 0.48 g (43%) of yellow crystals with m.p. 178°.

Found %: N 13.61, 13.62; S 7.98, 8.03. $C_{16}H_{22}O_7N_4S$. Calculated %: N 13.52; S 7.74.

With stirring, 0.95 g of concentrated sulfuric acid was added dropwise to a cooled ether solution of 1.8 g of 7-methyl-5,7-diethyltetrahydrohepta-1,4-thiazine. The white oil which precipitated was washed with ether and dissolved in acetone. A solid mass precipitated after a few minutes of rubbing with a rod. Recrystallization from acetone yielded 0.26 g of the sulfate of the base as white crystals with m.p. 119°.

Found %: N 5.18, 5.12; S 22.87, 22.39. $C_{10}H_{21}O_4NS$. Calculated %: N 4.98; S 22.68.

7-Methyl-5,7-diethyltetrahydrohepta-1,4-thiazine (2 g) was mixed with 2 g of methyl iodide with cooling. When the exothermal reaction was complete, the mixture was left at room temperature for a few hours. The yellow oil formed was washed with dry benzene and ether. The oil crystallized when triturated with acetone. Recrystallization from isopropyl alcohol yielded 0.99 g (28%) of the iodomethylate with m.p. 143-144°.

Found %: I 38.61, 39.05. $C_{11}H_{22}NSI$. Calculated %: I 38.77.

5,7,7-Trimethyl-4-phenyltetrahydrohepta-1,4-thiazine. A mixture of 15.3 g (0.1 mole) of β-phenylaminoethyl mercaptan and 9.8 g (0.1 mole) of mesityl oxide was heated in a sealed tube on a boiling water bath for 10 hr. The reaction product was then dissolved in ether, washed with 10% alkali solution, and dried with sodium sulfate. After removal of the ether, the residue was vacuum distilled. The product distilled with decomposition.

Fractions were collected: 1st, 110-115° (0.1 mm), 4 g; 2nd, 115-140°, 6.7 g. These gave a positive reaction for a mercapto group. Quantitative analysis for nitrogen gave results which were 0.8-0.6% high for both fractions.

Pure 5,7,7-trimethyl-4-phenyltetrahydrohepta-1,4-thiazine was obtained from the recrystallized perchlorate by shaking the latter with an aqueous solution of sodium hydroxide. The oil liberated was extracted with ether, dried with sodium sulfate, and filtered and the ether removed in vacuum. The residual oil was pure base. From 1.4 g of perchlorate we obtained 0.89 g (91%) of pure base with d^{15}_4 1.0720, $n^{15}D$ 1.5601.

Found %: N 6.16, 6.22; S 13.61, 13.76. $C_{14}H_{19}NS$. Calculated %: N 6.02; S 13.74.

The phenylperchlorate of 5,7,7-trimethyltetrahydrohepta-1,4-thiazine was obtained from the second fraction in the following way. To an alcohol solution of 1.8 g of base was added perchloric acid to an acidic reaction. White crystals of the quaternary salt precipitated. Recrystallization from alcohol yielded 0.98 g (38%) of lustrous needles with m.p. 189.5°.

Found %: N 4.11, 3.93; Cl 10.63, 10.75. $C_{14}H_{20}O_4NSCl$. Calculated %: N 4.19; Cl 10.96.

Condensation of β-phenylaminoethyl mercaptan with methyl β-bromoisobutyl ketone. A mixture of 2 g (0.013 mole) of β-phenylaminoethyl mercaptan and 2.4 g (0.013 mole) of methyl β-bromoisobutyl ketone was heated in a sealed tube on a water bath for 3 hr. The thick oil obtained was washed with ether. It could not be crystallized. Therefore, an aqueous solution of sodium perchlorate was added to an alcohol solution

of the oil. Crystals of the quaternary salt precipitated after a few minutes. After recrystallization from alcohol the phenylperchlorate of 5,7,7-trimethyltetrahydrohepta-1,4-thiazine melted at 189°. The yield was 0.95 g (24%). This salt was found to be identical with the salt obtained from 5,7,7-trimethyl-4-phenyltetrahydrohepta-1,4-thiazine and perchloric acid.

5,7,7-Trimethyltetrahydrohepta-1,4-diazine. The information on this base in the abstract of [2] is too brief. We therefore synthesized it and determined its most important physical constants. From 12.5 g of ethylenediamine and 19.6 g of mesityl oxide, which were heated on a water bath for 15 min, we obtained by vacuum distillation at 60-61° (3 mm) 14 g (56%) of 5,7,7-trimethyltetrahydrohepta-1,4-diazine with d^{22}_4 0.9393, $n^{20}D$ 1.4808, and b.p. 175°.

Found %: N 19.82, 19.87. $C_8H_{16}N_2$. Calculated %: N 19.97.

Mixing alcohol solutions of 0.2 g of 5,7,7-trimethyltetrahydrohepta-1,4-diazine and 0.3 g of picric acid yielded the picrate. Recrystallization from methanol yielded 0.45 g (86%) of picrate with m.p. 184° (decomp.).

Found %: N 19.16, 19.20. $C_{14}H_{19}O_7N_5$. Calculated %: N 19.13.

To a cooled ether solution of 4 g of base was added 4.6 g of 60% perchloric acid dropwise. The oil liberated crystallized when triturated with acetone. Recrystallization from aqueous alcohol yielded 4.7 g (68%) of the perchlorate of 5,7,7-trimethyltetrahydrohepta-1,4-diazine with m.p. 158°.

Found %: Cl 14.71, 14.96. $C_8H_{17}O_4N_2Cl$. Calculated %: Cl 14.72.

A solution of 5 g of 5,7,7-trimethyltetrahydrohepta-1,4-diazine in 15 ml of dry acetone was mixed with 5.6 g of methyl iodide. Heat was evolved and after a few minutes, white crystals of the salt precipitated. After recrystallization from methanol, the quaternary salt melted with decomposition at 152°. The yield was 3.5 g (35%).

Found %: N 10.32, 10.01; I 44.66, 44.32. $C_9H_{19}N_2I$. Calculated %: N 9.93; I 44.92.

A solution of 2 g of 5,7,7-trimethyltetrahydrohepta-1,4-diazine in 10 ml of dry acetone was mixed with 2.5 g of ethyl iodide. White crystals of the quaternary salt precipitated after a short time. Recrystallization from alcohol yielded 1.1 g (26%) of the iodoethylate of 5,7,7-trimethyltetrahydrohepta-1,4-diazine with m.p. 141-142°.

Found %: N 9.40, 9.51; I 42.61, 42.73. $C_{10}H_{21}N_2I$. Calculated %: N 9.46; I 42.86.

7-Methyl-5,7-diethyltetrahydrohepta-1,4-diazine. 7.2 g (0.12 mole) of ethylene diamine and 15.1 g (0.12 mole) of 3-methylhepten-3-one-5 were mixed. At first the liquids were immiscible. They were heated on a boiling water bath for 3 hr until they formed a homogeneous mixture. The reaction product was then dissolved in ether and dried with potassium hydroxide. After removal of the ether, the residue was vacuum distilled. The fraction collected at 93-95° (5 mm) was pure 7-methyl-5,7-diethyltetrahydrohepta-1,4-diazine. The yield was 12.2 g (60%) and the product had d^{20}_4 0.9298, $n^{20}D$ 1.4850.

Found %: N 16.51, 16.43. $C_{10}H_{20}N_2$. Calculated %: N 16.65.

The picrate formed yellow platelets with m.p. 261-262° (decomp.) (from alcohol).

Found %: N 17.68, 17.49. $C_{16}H_{23}O_7N_5$. Calculated %: N 17.63.

To a cooled ether solution of 1.68 g of 7-methyl-5,7-diethyltetrahydrohepta-1,4-diazine was added 1.7 g of 60% perchloric acid dropwise. The oil liberated was washed with ether and dissolved in acetone. After a short time the acetone solution deposited crystals of the perchlorate, which were recrystallized from alcohol, when they had m.p. 151-152°. The yield was 1.8 g (67%).

Found %: N 10.74, 10.76; Cl 13.02, 12.86. $C_{10}H_{21}O_4N_2Cl$. Calculated %: N 10.42; Cl 13.19.

A solution of 1.68 g of 7-methyl-5,7-diethyltetrahydrohepta-1,4-diazine in 8 ml of dry acetone was mixed with 1.42 g of methyl iodide. There was weak evolution of heat and after a few minutes white crystals of the quaternary salt precipitated. Recrystallization from alcohol yielded 0.55 g (18%) of the iodomethylate of 7-methyl-5,7-diethyltetrahydrohepta-1,4-diazine with m.p. 260°.

Found %: N 8.86, 8.96; I 40.98, 40.87. $C_{11}H_{23}N_2I$. Calculated %: N 9.03; I 40.89.

SUMMARY

The condensation of β-aminoethyl mercaptan, 2-mercaptopropylamine, β-phenylaminoethyl mercaptan, and ethylenediamine with mesityl oxide and 3-methylhepten-3-one-5 was studied. It was shown that the reaction products are seven-membered heterocyclic bases containing a nitrogen atom and a sulfur atom or two nitrogen atoms in positions 1 and 4 in the ring.

Four heterocyclic bases which have not been described in the literature were synthesized: 2,5,7,7-tetramethyltetrahydrohepta-1,4-thiazine, 7-methyl-5,7-diethyltetrahydrohepta-1,4-thiazine, 5,7,7-trimethyl-4-phenyltetrahydrohepta-1,4-thiazine, and 7-methyl-5,7-diethyltetrahydrohepta-1,4-diazine. Picrates, perchlorates, and quaternary salts were prepared from the bases.

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AROMATIC COMPOUNDS WITH A LONG SIDE CHAIN

III. REDUCTION OF ALKYL 4-AMINOPHENYL KETONES BY A MODIFICATION OF THE KIZHNER METHOD

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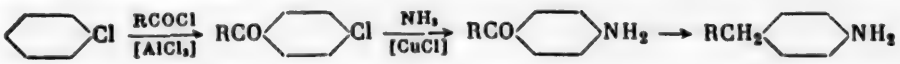
In the first communication [1] we showed that homologs of aniline with a normal aliphatic chain may be prepared according to the scheme:



The condensation and ammonolysis proceed smoothly and give good yields. However, reduction of aminophenyl alkyl ketones to C-alkylanilines with amalgamated zinc in hydrochloric acid by the Clemmensen method does not give steady yields. In addition, as we showed previously, the yield of alkylanilines falls with a decrease in the length of the aliphatic chain; the maximum yield (77.8 percent) was obtained for 4-octadecylaniline, but for 4-ethylaniline the yield was only 28.1%. In the present work, which is a continuation of the above investigation, we synthesized a series of mainly undescribed alkyl 4-chlorophenyl ketones and alkyl 4-aminophenyl ketones (R = C_2H_5, C_4H_9, C_6H_{13}, C_8H_{17}, C_9H_{19}, $C_{10}H_{21}$, $C_{13}H_{27}$, $C_{14}H_{29}$ and $C_{15}H_{31}$). The alkyl 4-aminophenyl ketones were reduced with hydrazine hydrate in triethylene glycol by a modification of Kizhner' method [2]. The yields of 4-alkylanilines were 75-85%.

EXPERIMENTAL

Preparation of alkyl 4-chlorophenyl ketones. Into a three-necked flask with a reflux condenser, thermometer, and stirrer was placed a solution of 0.2 mole of aliphatic acid chloride in 200 ml of dry chlorobenzene and 0.25 mole of anhydrous aluminum chloride added to it with stirring. The mixture was stirred for 2 hr at 20-22° and then for 1 hr at 100°. The mass was then poured into 1 liter of ice water and the excess chlorobenzene steam distilled. The chlorophenyl alkyl ketone was collected by filtration, dried in air, and recrystallized from methanol or ethanol. The alkyl 4-chlorophenyl ketones formed colorless scales; the 2,4-dinitrophenylhydrazones, which were obtained by the usual method, formed yellow to orange crystals, usually in the form of leaflets or platelets. The results of the experiments are given in Table 1.

Exchange of chlorine for an amino group. A mixture of 0.1 mole of alkyl 4-chlorophenyl ketone, 100-150 ml of 30% ammonia solution, and 0.02-0.03 mole of cuprous chloride was heated for 6 hr at 250-270° in a 0.25-liter rotating autoclave. The product was isolated by filtration, dried in air and recrystallized from methanol or ethanol. The alkyl 4-aminophenyl ketones were slightly yellowish scales and leaflets. Acetyl or benzoyl derivatives were prepared for identification purposes. The results of the experiments are given in Table 2.

Reduction of alkyl 4-aminophenyl ketones. Into a two-necked flask with a reflux condenser and thermometer were placed 0.1 mole of alkyl 4-aminophenyl ketone, 75 g of triethylene glycol, 0.3 mole of hydrazine

TABLE 1

Alkyl 4-Chlorophenyl Ketones $RCOC_6H_4Cl$-p

Nature of R	Yield (in %)	Melting point	Analysis data (in %) (calculated values are given in parentheses)	Melting point of 2,4-dinitrophenyl hydrazone
C_2H_5	58	34—35° [3]	—	
C_4H_9	80	32—32.5	C 66.89, 67.07 (67.17); H 6.82, 6.81 (6.66)	175—175.3°
C_6H_{13}	94	64.5—65.5	C 69.62, 69.67 (69.47); H 7.59, 7.70 (7.63)	150—151
C_8H_{17}	97	58—58.5	Cl 13.59, 13.62 (14.03)	134—135
C_9H_{19}	97	48—49 [4]	—	
$C_{10}H_{21}$	98	46.5—47	Cl 13.00, 13.04 (12.67)	103.5—104.5
$C_{13}H_{27}$	99	64.5—65 [1]	—	
$C_{14}H_{29}$	81	51.5—52	Cl 10.12, 9.95 (10.52)	80.3—80.7
$C_{15}H_{31}$	91	69.5—70	C 75.30 (75.28); H 10.30 (10.05)	100—100.6

TABLE 2

Alkyl 4-Aminophenyl Ketones

Nature of R	Yield (in %)	Melting point	% N	
			found	calculated
C_2H_5	86	137.5—138.5° [5]	—	—
C_4H_9	98	74—75 [5]	—	—
C_6H_{13} a	95	90—90.5	6.99, 7.06	6.83
C_8H_{17} b	98	91—92	6.21, 6.01	6.00
C_9H_{19}	97	97.5—98.5 [4]	—	—
$C_{10}H_{21}$	98	101.5—102	5.62, 5.70	5.36
$C_{13}H_{27}$ c	98	104—104.5	4.80, 4.88	4.62
$C_{14}H_{29}$	95	102—102.5	4.68, 4.57	4.41
$C_{15}H_{31}$ d	99	99—100	4.33, 4.50	4.23

a) 4-Acetylaminoenanthophenone, m.p. 123.5-124.5°. Found %: N 5.92, 5.78. $C_{15}H_{21}O_2N$. Calculated %: N 5.66.

b) 4-Benzoylaminopelargophenone, m.p. 151.5-151.8°. Found %: N 3.78, 3.91. $C_{22}H_{27}O_2N$. Calculated %: N 4.15.

c) 4-Benzoylaminomyristophenone, m.p. 146.3-146.7°. Found %: N 3.85, 3.93. $C_{27}H_{37}O_2N$. Calculated %: N 3.43.

d) 4-Acetylaminopalmitophenone, m.p. 111-111.5°. Found %: N 3.58, 3.70. $C_{24}H_{39}O_2N$. Calculated %: N 3.75.

hydrate, and 0.3 mole of powdered potassium hydroxide. The mixture was heated at 120-125° for 2 hr. The reflux condenser was then replaced by a distillation condenser, the temperature of the reaction mixture raised to 200-210°, and water distilled. The mass was heated at this temperature under reflux for 4 hr and then poured into cold water and the amine extracted with ether. After the ether solution had been dried over baked sodium sulfate, the solvent was removed and the amine vacuum distilled. The acetyl and benzoyl derivatives were prepared by the normal methods. The previously undescribed amines and their derivatives were analyzed for nitrogen. The melting and boiling points of the known substances agreed with literature data within the limits of the determination.

The results of the reduction experiments are given in Table 3.

TABLE 3

4-Alkylanilines $RC_6H_4NH_2$-p

Nature of R	Yield (in %)	Boiling point (pressure in mm) and melting point	Melting point of derivatives	
			acetyl	benzoyl
C_2H_5	67.3	214—216° [6]		151.3—151.8°
C_3H_7	75	112 (20) [7]		114—114.5 [8]
C_5H_{11}	84	128—130 (16) [9]	100—101° [9]	—
C_7H_{15}	84	160 (17) [9]	91—92 [9]	
C_9H_{19} a	80	194—196 (16)		114—115
$C_{11}H_{23}$ b	85	167—168 (3)	97—97.5	
		M.p. 19.5—20		
$C_{14}H_{29}$ c	98	M.p. 44.5—45		117—117.5
$C_{16}H_{33}$	—	M.p. 52—52.2 [9]	105 [9]	

a) Benzoyl derivative. Found %: N 4.11, 4.28. $C_{22}H_{29}ON$. Calculated %: N 4.33.

b) Acetyl derivative. Found %: N 4.53, 4.70. $C_{19}H_{31}ON$. Calculated %: N 4.84.

c) 4-Tetradecylaniline. Found %: N 4.93, 5.02. $C_{20}H_{31}N$. Calculated %: N 4.68. Benzoyl derivative. Found %: N 3.64, 3.80. $C_{27}H_{39}ON$. Calculated %: N 3.47.

SUMMARY

1. 4-Chloropropio-, -valero-, -enantho-, -pelargo-, -capro-, -undecano-, -myristo-, and -palmitophenones were synthesized by condensation of aliphatic acid chlorides with chlorobenzene; ammonolysis of these yielded the corresponding alkyl 4-aminophenyl ketones.

2. The reduction of alkyl 4-aminophenyl ketones with hydrazine hydrate by a modification of the Kizhner method was studied. The yields of alkylanilines reached 90%.

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HYDROGENATION PRODUCTS OF PYRIDINE CHLOROPHENYLATE

CONDENSATION OF N-PHENYLPIPERIDINE HYDROCHLORIDE WITH p-DIMETHYLAMINOBENZALDEHYDE

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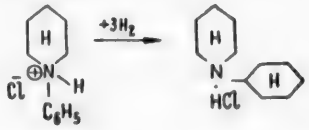
It was previously reported that N-arylpyridine salts are readily hydrogenated over a platinum catalyst at normal temperature [1]. From the amount of hydrogen absorbed and analysis data it was considered that the hydrogenation products are N-arylpiperidine salts. It was reported that these salts are capable of condensing. Further investigation showed that the hydrogenation of pyridine chlorophenylate forms a mixture of two salts whose ratio depends on the hydrogenation conditions, namely, the amount of catalyst and the hydrogenation time. The hydrogenation rate decreases sharply when about 3 moles of hydrogen have been absorbed. If the hydrogenation is stopped after the sharp decrease in the hydrogen absorption rate then the main product is a salt with m.p. 207°, which gives a color reaction with p-dimethylaminobenzaldehyde. The base from the salt is a colorless oil with a sharp, specific smell, whose picrate has m.p. 148.5° and hydrobromide m.p. 136°, which coincide with literature data for N-phenylpiperidine [2]. Exhaustive hydrogenation of pyridine chlorophenylate or rehydrogenation of the N-phenylpiperidine salt yields a salt with m.p. 283°. This salt does not give a color reaction with p-dimethylaminobenzaldehyde. According to the amount of hydrogen absorbed, analysis data, and the melting point of the picrate, this salt is N-cyclohexylpiperidine hydrochloride [3].

Hydrogenation of the benzene ring in the N-phenylpiperidine salt under mild conditions is possible due to the electrophilic effect of the ammonium radical.



N-Phenylpiperidine in the form of the base is not hydrogenated under analogous conditions.

Condensation of N-phenylpiperidine hydrochloride with p-dimethylaminobenzaldehyde in acetic anhydride formed first a blue dye, which decomposed rapidly on heating to form a red dye. We were unable to isolate the blue dye, but the fact that it was an intermediate and not a byproduct of the condensation was demonstrated by the following observations. Preliminary experiments established that the highest yield of dye was obtained when a molecular mixture of salt and aldehyde in a ratio of 1 : 2 was used in the condensation. It was shown spectroscopically that with heating there was a decrease in the intensity of the band with an absorption maximum at 603 mμ and an increase in the intensity of the band with a maximum at 500-504 mμ (Fig. 1).

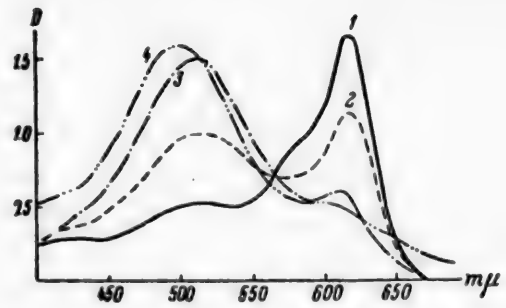


Fig. 1. Change in color with time during the condensation of N-phenylpiperidine hydrochloride with p-dimethylaminobenzaldehyde in acetic anhydride. 1) Absorption curves of acetic anhydride solution at the beginning of condensation; 2) the same after the mixture had been heated for 20 min; 3) the same after 30-min heating; 4) the same after heating to constant color.

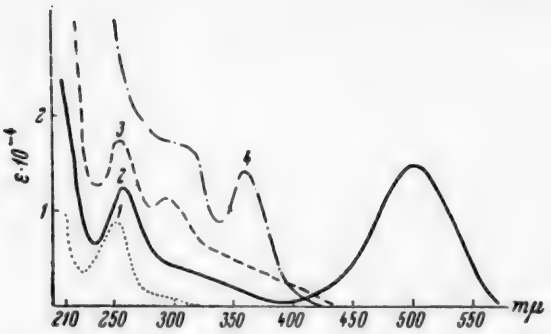
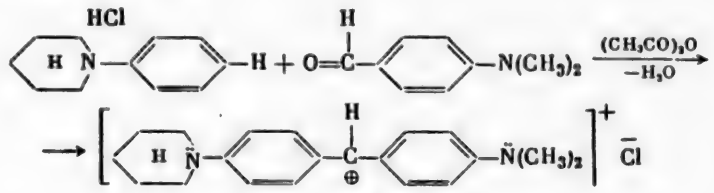


Fig. 2. Absorption spectra of N-phenylpiperidine hydrochloride and the product of its condensation with p-dimethylaminobenzaldehyde (red dye). 1) N-Phenylpiperidine hydrochloride in methanol; 2) dye in methanol; 3) the same + excess alkali; 4) the same + excess hydrochloric acid.

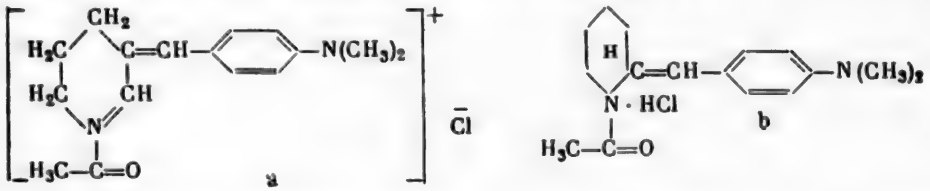
The blue dye was not formed by condensation of N-phenylpiperidine (base) with p-dimethylaminobenzaldehyde under analogous conditions. The reaction mixture acquired a red color when heated, but it was impossible to isolate the dye, which was formed in insignificant amounts.

Under analogous conditions, p-dimethylaminobenzaldehyde will condense with other N-substituted pyridine salts containing substituents (OCH_3, $COOC_2H_5$, NH_2) in the para positions in the benzene rings to form red dyes with the same color as the unsubstituted salt. The intermediate blue dye was not formed during the condensation of these salts.

The color of the intermediate blue dye was close to that of Michler's benzhydrol [4] and it is extremely probable that it is an analog of the latter.



Successively or simultaneously with the first, there is an oxidation-reduction condensation with the second aldehyde molecule. The heightening of the color by 100 mμ cannot be connected with the introduction of a second p-dimethylaminobenzene radical; it may be connected with the replacement of the complex radical at the heteroatom by a simple one, for example, an acetyl group. It is possible that the entry of the complex radical into the hydrogenated pyridine nucleus forms a styril of structure a or b.



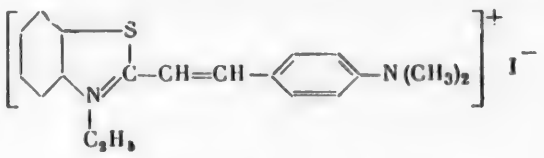
The structure for the red dye expressed by formula a seemed more probable to us. The terminal amine groups are conjugated in this structure and it is understandable why the dye is decolorized by the action of excess alkali or acid (Fig. 2).

TABLE 1

Expt. No.	Amount			Change of hydrogenation rate with time (ml of H_2 per min)					Total hydrogen absorbed		Duration of hydrogenation (in min)
	starting salt (in g)	catalyst (in g)	alcohol (in ml)	15′	20′	20′	10′	60′	(in ml)	(in mole)	
				Methanol as solvent							
1	10	0.25	200	53	63	67	—	—	3560	3.2	65
2	5	0.25	100	70	51	10	6	—	2350	4.2	65
3	3	0.15	60	15	23	23	15	6	2000	6.0	660
				Ethanol as solvent							
4	2	0.2	60	20	18	12	3	1.5	1180	5.3	280
5	2	0.1	60	12	14	6	3	2.5	800	3.6	160
6	4	0.2	120	20	35	35	5	—	1850	4.2	100

The red dye was sparingly soluble in water, but more soluble in alcohol and dichloroethane. The dye did not crystallize and did not have a sharp melting point. The absorption maximum was at 496 mμ in alcohol, 504 mμ in water, and 504 mμ in dichloroethane. The dye was isolated as the chloride or acetate.

The dye obtained condensed with 2-methylbenzthiazole iodoethylate to form a known styril dye [5].



This reaction indirectly confirms the structure of the red dye we obtained and the fact that it is a dye of the styril type. In addition, had there not been oxidation of the piperidine ring or other conversions during the condensation, then during the condensation of the dye with 2-methylbenzthiazole iodoethylate the N-phenylpiperidine should have been displaced and it could have been identified.

EXPERIMENTAL

The hydrogenation of pyridine chlorophenylate was carried out by the procedure described previously [1]. Experiments on the hydrogenation of pyridine chlorophenylate under various conditions are presented in Table 1.

The rate of hydrogen absorption and the degree of hydrogenation (amount of hydrogen absorbed) depended on the amount of catalyst and the duration of hydrogenation (experiments 1, 2, 4, and 5). With the same ratio of catalyst and solvent, the hydrogen absorption rate and degree of hydrogenation increased with an increase in the amount of starting salt (experiments 5 and 6). The hydrogenation rate was slightly greater in methanol than in ethanol, which was connected with the higher solubility of the starting salt in methanol. The amount of solvent had an appreciable affect on the hydrogenation rate; concentrated solutions of salt were hydrogenated slowly even with an increase in the amount of catalyst.

After removal of the catalyst, the alcohol was distilled with a fractionating column and the residual alcohol slowly evaporated on a water bath. The product was dried in a vacuum desiccator and recrystallized from anhydrous alcohol and ether (1 : 4) with charcoal to yield salts with sharp melting points; otherwise the recrystallization was repeated. Treatment of the mother liquors with absolute ether yielded mixtures of salts with indefinite melting points.

One salt with m.p. 207° was identified in experiments 1 and 5 (Table 1). The base from the salt was a colorless oil with a sharp, specific smell. After two recrystallizations from an alcohol-water mixture (1 : 4), the picrate melted at 148.5°. The hydrobromide formed lustrous platelets from alcohol and had m.p. 236°.

Salt. Found %: N 7.07, 7.10. $C_{11}H_{16}NCl$. Calculated %: N 7.09.

Picrate. Found %: N 14.24, 14.42. $C_{17}H_{18}O_7N_4$. Calculated %: N 14.36.

Hydrobromide. Found %: N 5.69, 5.71. $C_{11}H_{16}NBr$. Calculated %: N 5.78.

The product of exhaustive hydrogenation of pyridine chlorophenylate (expt. 3) did not give a color reaction with p-dimethylaminobenzaldehyde; two recrystallizations from anhydrous alcohol yielded a salt with m.p. 283°. The base was a colorless oil without smell. After two recrystallizations from water, the picrate melted at 128°. The nydrobromide formed lustrous scales from alcohol and had m.p. 297°.

Salt. Found %: N 7.01, Cl 17.50. $C_{11}H_{22}NCl$. Calculated %: N 6.88; Cl 17.44.

Picrate. Found %: N 14.10. $C_{17}H_{24}O_7N_4$. Calculated %: N 14.14.

Hydrobromide. Found %: N 5.82; Br 32.16. $C_{11}H_{22}NBr$. Calculated %: N 5.65; Br. 32.26.

Rehydrogenation of N-phenylpiperidine hydrochloride. A sample (0.6 g) of salt with m.p. 207° in 15 ml of methanol with 0.05 g of platinum dioxide was hydrogenated until the absorption of hydrogen ceased. After 6 hr, 230 ml of hydrogen (approximately 3 moles) had been absorbed. We obtained 0.54 g of an almost colorless, crystalline product; after recrystallization from anhydrous alcohol it melted at 283°; the picrate had m.p. 128° and did not depress the melting point of the picrate of the product from exhaustive hydrogenation.

Recrystallization of the hydrogenation products from experiments 2, 4, and 6 (Table 1) yielded salts with m.p. 207 and 238°; treatment of the mother liquors with excess dry ether precipitated mixtures with various melting points. According to the nitrogen and chlorine contents, they were close to the salts of N-phenyl- and N-cyclohexylpiperidine, but it was impossible to separate them by recrystallization. The percent of N-phenylpiperidine hydrochloride in these mixtures was determined spectroscopically. A mixture of 0.01 g of salt and 0.015 g of p-dimethylaminobenzaldehyde in 1 ml of acetic anhydride was heated to a constant red-violet color and then the reaction mixture diluted to 250 ml with methanol and the absorption curves determined. The optical density (D) of the band with an absorption maximum at 496 mμ was used to calculate the dye content of the solution and hence the N-phenylpiperidine salt content. The results of these experiments are given in Table 2.

Condensation of N-phenylpiperidine hydrochloride with p-dimethylaminobenzaldehyde. Expt. 1. A mixture of 1.4 g (1 mole) of salt and 2.1 g of p-dimethylaminobenzaldehyde (2 moles) in 5 ml of acetic anhydride was boiled for 1 hr. Immediately after heating, the thick solution acquired a green color and then an intense blue color, which changed to a constant red with heating. The cooled mixture was extracted repeatedly with ether. The greasy, red residue was dissolved in water and the dye precipitated with a saturated solution of sodium chloride, washed repeatedly with water, and dried. Part of the dye dissolved in water during the washing. We obtained 0.65 g of a finely crystalline, red powder. To remove traces of sodium chloride, the vacuum-dried dye was dissolved in anhydrous methanol, the solution filtered, and the dye precipitated with absolute ether. The dye was sparingly soluble in water, readily soluble in acetic acid, and less soluble in methanol, ethanol, dichloroethane, and acetone. It decomposed without melting when heated.

Found %: C 64.17, 64.60; H 7.46, 7.38; N 9.77, 9.65; Cl 12.70, 12.65. $C_{16}H_{21}ON_2Cl$. Calculated %: C 65.65; H 7.18; N 9.73; Cl 12.14.

Experiment 2. A mixture of 1 g of salt, 1.5 g of p-dimethylaminobenzaldehyde, and 12 ml of acetic anhydride was boiled for 1.5 hr. At the beginning of heating, the solution acquired an intense blue color, which rapidly changed to red-violet and then a constant red. The mixture was poured into ether (about 100 ml). The precipitate was washed with ether and dried. We obtained 1.2 g of a dark red powder. Reprecipitation from anhydrous alcohol with dry ether yielded a bright red, finely crystalline product (1.7 g). The dye contained solvent of crystallization. For the removal of possible traces of starting salt, 50 ml of water was added to 1.7 g of the dye, when part of the dye dissolved in the water. The residue was washed with water on a filter and as the salt was washed out, the solubility of the dye decreased. We obtained 0.78 g of washed and dried dye. The dye which dissolved during the washing was precipitated with sodium chloride and repeatedly washed with water to yield a further 0.6 g of dye. The dye was dried in vacuum (40 mm, 65°) over P_2O_5 for 2 hr before analysis. After grinding, the dark red powder decomposed without melting, did not contain chlorine, and did not separate

TABLE 2

Melting point of starting salt	Optical density (D)	N-Phenylpiperidine hydrochloride content of mixture (in %)
150-165*	0.5	28.6
175-185	1.1	64.3
190-200	1.3	74.3
207	1.75	100

into zones on an absorption column. The dye differed little in solubility from the chloride obtained in Expt. 1 and gave the same color in different solvents. Alcohol solutions of the dye were decolorized by excess alkali and concentrated hydrochloric acid.

Found %: N 8.90, 8.96. $C_{18}H_{24}O_3N_2$. Calculated %: N 8.86.

The base of the dye was formed by the action of alkali on an aqueous suspension. After the addition of alkali, the red color disappeared and the almost colorless, flocculent precipitate coagulated and was centrifuged and washed repeatedly with water to a neutral reaction. When dried in a desiccator on a earthenware plate over alkali, it appeared as a dirty yellow, amorphous substance. The base was sparingly soluble in alcohol and an alcohol solution had a red color with an absorption maximum at 504 mμ. The base was readily soluble in benzene to give a yellow solution; treatment with charcoal and precipitation with excess ligroin yielded an almost colorless precipitate, but it rapidly turned pink during filtration. After the substance had been dried in vacuum, a test for solvent of crystallization was negative.

Found %: N 8.77, 8.94. $C_{16}H_{22}O_2N_2 \cdot CO_2$. Calculated %: N 8.81.

A bright red, flocculent precipitate of the dye was formed by treatment of a benzene solution with hydrogen chloride. The absorption maximum of an alcohol solution was 496 mμ and of an aqueous solution, 504 mμ.

Condensation of red dye with 2-methylbenzthiazole iodoethylate. A mixture of 1 g of dye (chloride) and 1.2 g of 2-methylbenzthiazole iodoethylate in 10 ml of pyridine was heated on a mantle for 2 hr. A dark crystalline precipitate was deposited by the thick, red-violet solution. Recrystallization from alcohol yielded lustrous violet crystals with m.p. 230° (0.8 g). The absorption maximum in alcohol of 535 mμ coincided with the maximum of the dye obtained by condensation of 2-methylbenzthiazole iodoethylate with p-dimethylaminobenzaldehyde. A mixed melting point of the two dyes was not depressed.

Found %: N 6.35. $C_{19}H_{21}SN_2I$. Calculated %: N 6.44.

SUMMARY

1. It was established that hydrogenation of pyridine chlorophenylate over a platinum catalyst forms a mixture of N-phenyl- and N-cyclohexylpiperidine hydrochlorides whose ratio depends on the hydrogenation conditions.

2. N-phenylpiperidine hydrochloride condenses with p-dimethylaminobenzaldehyde to form a red dye. It is considered that the dye is the salt of N-acetyl-β-(p-dimethylaminostyryl)-1,2,3,4-tetrahydropyridine.

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SYNTHESIS OF ESTERS OF UNDECYLENIC ACID AND SOME OF ITS DERIVATIVES

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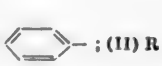
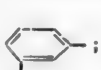
In connection with the recent communication [1] on the application of phenyl undecylenate (I) in the treatment of various forms of fungus diseases, it seemed interesting to synthesize for testing other aromatic esters of this acid, namely, the m-cresyl (II), thymyl (III), and guaiacyl (IV) esters. For comparison of the activity, we also synthesized phenyl undecylenate (I) and methyl 11-phenoxy-10-hydroxyundecanoate (V).

Esters (I) to (IV) were synthesized by the general method, namely, condensation of undecylenyl chloride with the appropriate substituted phenols.

$$CH_2{=}CH(CH_2)_8COOR;$$

(I) R =  ; (II) R =  ; (III) R = ; (IV) R = ;

$$C_6H_5OCH_2CHOH(CH_2)_8COOCH_3$$
(V)

It should be noted that the preparation of esters (II) and (IV) required a condensation temperature of 160°, the preparation of (III) required 200°, while room temperature was sufficient for the preparation of (I). According to literature data [2, 3], phenyl undecylenate is obtained at a higher temperature.

An attempt to prepare the nitrophenyl esters of undecylenic acid by the same method did not lead to a positive result; when undecylenyl chloride was heated with o-, m-, and p-nitrophenols and 2,6-dinitrophenol at various temperatures (from 100 to 250°), no reaction occurred and the starting materials were recovered. The presence of the nitro group in the benzene nucleus apparently hinders this reaction. An attempt to prepare m-nitrophenyl undecylenate from sodium undecylenate and m-chloronitrobenzene was also unsuccessful.

We also prepared phenyl undecylenate (I) by heating undecylenic acid with phenol and phosphorus pentachloride. In this case the reaction did not proceed in one direction only and as a byproduct we obtained a 21% yield of undecalactone, which we synthesized for comparison from undecylenic acid and sulfuric acid [4].

Methyl 11-phenoxy-10-hydroxyundecanoate (V) was synthesized from methyl 11-chloro-10-hydroxyundecanoate [5] and sodium phenolate in alcohol.

EXPERIMENTAL

Phenyl undecylenate. A mixture of 18.4 g of phenol and 40 g of technical, undistilled undecylenyl chloride was stirred at room temperature for 4 hr; then the unreacted undecylenyl chloride was removed in vacuum and the residue distilled. The yield of phenyl undecylenate was 38.6 g (75%).

B.p. 193-195° at 11 mm. According to literature data [2]: b.p. 168-170° at 1.5 mm, $n^{20}D$ 1.4903, d_{20}^{20} 0.9594, MR_D 78.36; calc. 78.29.

m-Cresyl undecylenate. A mixture of 20 g of m-cresol and 37 g of undecylenyl chloride was stirred at room temperature for 1 hr, on a boiling water bath for 1 hr, and then at 160° until the evolution of hydrogen chloride ceased completely. Ether was added to the cooled reaction solution and then the ether solution was washed with water, sodium bicarbonate, and again with water, and dried with sodium sulfate. After removal of the solvent, the residue was vacuum distilled. The yield of m-cresyl undecylenate was 30 g (60%).

B.p. 175° at 0.3 mm, $n^{20}D$ 1.4902, d_{20}^{20} 0.9713, MR_D 81.65; calc. 82.91.

Found %: C 78.33; H 9.53. $C_{18}H_{26}O_2$. Calculated %: C 78.78; H 9.55.

Thymyl undecylenate. A mixture of 11.1 g of thymol and 15 g of undecylenyl chloride was heated with stirring on an oil bath at 180-200° until the evolution of gas ceased. The same treatment procedure was used. The yield of thymyl undecylenate was 11.5 g (50%).

B.p. 208-210° at 3 mm, $n^{20}D$ 1.4885, d_{20}^{20} 0.9473, MR_D 96.22; calc. 96.76.

Found %: C 79.25; H 10.00. $C_{21}H_{32}O_2$. Calculated %: C 79.69; H 10.19.

Guaiacyl undecylenate. A mixture of 10 g of guaiacol and 16.3 g of undecylenyl chloride was stirred and heated on a boiling water bath for 1 hr and then at 160° until the evolution of hydrogen chloride ceased completely. Treatment was carried out as in the previous experiment. The yield of guaiacyl undecylenate was 12.6 g (55%).

B.p. 187-189° at 4.5 mm. According to literature data [3]:• b.p. 219-221° at 11 mm, $n^{20}D$ 1.4950, d_{20}^{20} 1.0028, MR_D 84.33; calc. 84.55.

Found %: C 74.54; H 8.55. $C_{18}H_{26}O_3$. Calculated %: C 74.44; H 8.52.

Reaction of undecylenic acid, phenol, and phosphorus pentachloride. Phosphorus pentachloride (28 g) was added in portions to a mixture of 74 g of undecylenic acid, 38 g of phenol, and 200 ml of benzene. The reaction mixture was stirred first at room temperature for 4 hr and then at 120° until the evolution of hydrogen chloride ceased completely. After the usual treatment, the ether was removed by distillation and the residue fractionated in vacuum. We obtained 39 g (21%) of undecalactone with b.p. 158-159° at 7 mm (according to literature data [4]: b.p. 286° at normal pressure) and 50 g of phenyl undecylenate with b.p. 182-184° at 7 mm. The undecalactone obtained was identical with undecalactone synthesized by the procedure in [4].

Methyl 11-phenoxy-10-hydroxyundecanoate. A solution of 5 g of methyl 11-chloro-10-hydroxyundecanoate [5] in 20 ml of anhydrous alcohol was added with stirring to a solution of 2.8 g of phenol and 0.45 g of metallic sodium in 40 ml of anhydrous alcohol. The reaction solution was boiled for 16 hr. After removal of the solvent in vacuum, water was added to the residue and the precipitate collected, washed with water, and dried. After two recrystallizations from methanol, the substance had m.p. 66-67°.

Found %: C 69.92; H 9.07; OH 5.82. $C_{18}H_{28}O_4$. Calculated %: C 70.10; H 9.15; OH 5.51.

SUMMARY

1. The phenyl, m-cresyl, thymyl, and guaiacyl esters of undecylenic acid were synthesized by the usual method.

2. It was established that in the reaction of undecylenic acid with phenol and phosphorus pentachloride, in addition to the formation of phenyl undecylenate, lactonization of undecylenic acid occurs.

3. Methyl 11-phenoxy-10-hydroxyundecanoate was synthesized.

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SYNTHESIS OF MERCAPTO AMINO COMPOUNDS

IV. SYNTHESIS OF β-MERCAPTOETHYLAMINE AND 1-AMINO-2-MERCAPTOBUTANE

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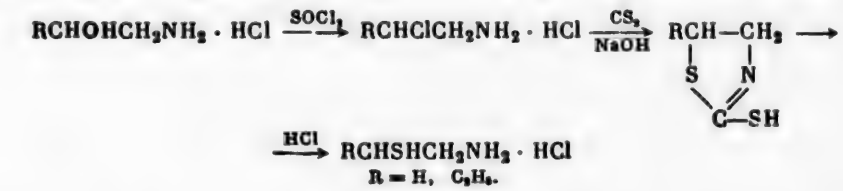
In the present work we describe the synthesis of β-mercaptoethylamine and 1-amino-2-mercaptobutane by a scheme that one of us used previously for the preparation of 3-mercapto-4-amino-2-methylbutane [1].



$$RCHOHCH_2NH_2 \cdot HCl \xrightarrow{SOCl_2} RCHClCH_2NH_2 \cdot HCl \xrightarrow[NaOH]{CS_2} RCH(S)CH_2(N)C{=}S \xrightarrow{HCl} RCHSHCH_2NH_2 \cdot HCl$$

R = H, C_2H_5.

The synthesis of β-mercaptoethylamine through 2-mercaptothiazoline was described in 1897 [2]. However, this method does not give the mercapto amine in satisfactory yield or of the required quality. 2-Mercaptothiazoline is obtained in a yield of no higher than 10% by condensation of carbon disulfide with ethanolamine under the conditions described by Knorr [3]. The synthesis from β-bromoethylamine hydrobromide is more satisfactory [4]; however, this synthesis involves certain experimental difficulties in the preparation of the starting compound. We found conditions under which β-mercaptoethylamine hydrochloride is obtained by the scheme given above in 42% yield (calculated on ethanolamine); all stages of the synthesis were refined and simplified.

It was found that the result of the synthesis depends on the quality of the β-chloroethylamine hydrochloride. It was established that the latter is obtained in high quality and in 98% yield by the action of thionyl chloride on ethanolamine hydrochloride in dichloroethane at 50-60° with heating for 2 hr, while the action of thionyl chloride on ethanolamine or its hydrochloride at a higher temperature forms a tarry, unfilterable substance, which apparently contains a large amount of hydrochlorides of ethanolamine polymerization products.

The condensation of crystalline β-chloroethanolamine hydrochloride (1 mole) and carbon disulfide (1.3 mole) in the presence of alkali (2 mole) in alcohol gave a 60% yield of 2-mercaptothiazoline, which was boiled with 20% hydrochloric acid for 50 hr to give β-mercaptoethylamine hydrochloride in 71.5% yield.

The method we developed for the preparation of β-chloroethylamine hydrochloride may be used in the synthesis of ethyleneimine [5]; the latter is then obtained in 50.6% yield (on the starting ethanolamine).

For the preparation of β-mercaptobutylamine, which has not been described in the literature, 1-nitro-2-hydroxybutane (prepared by condensation of nitromethane with propionaldehyde [6]) was reduced at room temperature in an autoclave in the presence of Raney nickel to 1-amino-2-hydroxybutane. By the action of thionyl chloride in dichloroethane, the hydrochloride of the latter was converted into the corresponding chloride. The action of carbon disulfide on this chloride yielded 2-mercapto-5-ethylthiazoline, which was heated with concentrated hydrochloric acid in a sealed tube at 180-190° for 5 hr to give 1-amino-2-mercaptobutane hydrochloride.

In the literature there is a communication on the synthesis of 2-mercapto-5-ethylthiazoline from bromobutylamine hydrobromide by the action of carbon disulfide [7]; however, neither the constants nor the complete analysis of this compound were given.

In the development of hydrolysis conditions for the 5-alkylthiazolines we synthesized, it was established that the hydrolysis of 2-mercaptothiazoline requires 50-hr boiling with 20% hydrochloric acid. 5-Methyl-2-mercaptothiazoline is hydrolyzed under the same conditions with 90-100-hr boiling; the isopropyl [1] and ethyl homologs of 2-mercaptothiazoline are cleaved only by heating with concentrated hydrochloric acid in sealed tubes; the most resistant to hydrolysis is 2-mercapto-5-ethylthiazoline, which is cleaved only at 185-190°.

EXPERIMENTAL

Ethanolamine hydrochloride. Over a period of 1-1.5 hr, 200 g of technical 90% monoethanolamine was added with stirring to 360 ml of technical hydrochloric acid at 15-50°. The reaction solution was evaporated to dryness in vacuum. The yield of monoethanolamine hydrochloride as a clear sirup which crystallized on cooling was 300 g. The melting point of the technical product was 79-82°. According to literature data [8], m.p. about 100°.

β-Chloroethylamine hydrochloride. To the hot, sirupy product from the previous stage was added 300 ml of dry dichloroethane, which was removed by distillation at atmospheric pressure in order to remove moisture. To the residue was added 600 ml of fresh dry dichloroethane and then 288 ml of thionyl chloride was added with stirring over 30-40 min, when a precipitate formed. When the thionyl chloride had been added, the reaction mixture was stirred for 1 hr at room temperature and then for 3-4 hr at 50-60°. After 1.5 hr of heating, the reaction mixture became liquid and then a precipitate formed again. After cooling, the precipitate was collected by filtration, washed with dry dichloroethane, and dried in a drying cupboard at 100°. We obtained 342 g of material containing 98% of chloroethylamine hydrochloride. The yield was 98%, calculated on monoethanolamine. The melting point of the technical product was 141-144°, which corresponds to literature data [9].

2-Mercaptothiazoline. To a solution of 342 g of 98% β-chloroethylamine hydrochloride in 400 ml of water was added 227 g of sodium hydroxide in 600 ml of water. Carbon disulfide (222 ml) was gradually added to the solution obtained over a period of 30 min with stirring at a temperature of no higher than 30° and then 2000 ml of ethanol was added. The reaction mass was stirred until the temperature fell to room temperature (18-20°). After evaporation in vacuum, the dry residue was treated with 200 ml of water and the yellow precipitate collected, washed with water, and recrystallized from water (1 : 10). The yield of 2-mercaptothiazoline was 207 g (60%). It had m.p. 102.5-104.5°. According to literature data [4]: m.p. 106-107°.

β-Mercaptoethylamine hydrochloride. A mixture of 207 g of 2-mercaptothiazoline and 5000 ml of 20% hydrochloric acid was boiled for 50 hr on an oil bath. After evaporation of the solution in vacuum, the dry residue was dissolved in 3000 ml of anhydrous alcohol and the alcohol solution heated with charcoal and filtered. To the cooled alcohol filtrate was added dry ether until turbidity appeared. When kept at 0° for one day, the solution deposited a precipitate, which was collected and washed with a mixture of anhydrous alcohol and absolute ether (1 : 2). We obtained 151 g of a substance with m.p. 67-69°.

According to iodometric titration, the substance contained 93-95% of mercapto amine and 7-5% of disulfide. Analysis showed that the substance contained no other materials. The yield of β-mercaptoethylamine hydrochloride was 71.5%, calculated on 2-mercaptothiazoline.

Ethyleneimine. A solution of 342 g of 98% β-chloroethylamine hydrochloride in 600 ml of water, 225 g of sodium hydroxide, and 300 ml of water was heated with stirring on an oil bath and at 75° the distillation of ethyleneimine began and was continued until the temperature of the vapor reached 100°. The distillate was collected in an ice-cooled receiver with dry sodium hydroxide. At the end of the distillation the ethyleneimine was separated from the lower alkaline layer and dried with fused potassium hydroxide (30 g). After standing for several days, the ethyleneimine was separated from the potassium hydroxide and distilled over fused potassium hydroxide. The b.p. was 54-57°. The ethyleneimine yield was 62.3 g (51.7%, calculated c. the β-chloroethylamine hydrochloride). The alkaline solutions (after separation of the ethyleneimine) from several experiments were combined and further treatment with solid alkali after several days standing yielded an additional amount of ethyleneimine.

1-Amino-2-hydroxybutane. To 78.5 g of 1-nitro-2-hydroxybutane [6] in 150 ml of alcohol was added 10 g of Raney nickel. The hydrogenation was carried out at room temperature in an autoclave for 2 hr at an initial pressure of 160 atm. At the end of the hydrogenation, the catalyst was removed by filtration, the alcohol evaporated, and the residue vacuum distilled. The yield of 1-amino-2-hydroxybutane was 38.3 g (65%). It had b.p. 77-79° at 20 mm. According to literature data [6, 10]: b.p. 75-77° at 12 mm; 168-170° at normal pressure.

1-Amino-2-chlorobutane hydrochloride. To 14.1 g of 1-amino-2-hydroxybutane was added 159 ml of 1 N HCl solution and the solution obtained evaporated to dryness in vacuum. The sirup obtained (20 g) was cooled in ice water while 24 ml of thionyl chloride was added dropwise and then the reaction mixture was left at room temperature for 7 hr. To the liquid mass was added 100 ml of dry ether. The precipitate was collected, washed with dry ether, and dried in a vacuum desiccator. The yield of 1-amino-2-chlorobutane was 20 g (87%). The substance was not purified further due to its hygroscopic nature.

2-Mercapto-5-ethylthiazoline. With cooling in ice water and stirring, 9 ml of carbon disulfide and 45 ml of 40% NaOH were added to a solution of 20 g of 1-amino-2-chlorobutane hydrochloride in 150 ml of water (first purified by boiling with charcoal) at such a rate that the temperature did not rise above 90°. After being stirred at room temperature for 30 min, the solution was cooled with ice water and acidified with hydrochloric acid. The precipitate was collected and washed with water. The substance was purified by reprecipitation from an alkaline solution by hydrochloric acid with cooling. The yield of 2-mercapto-5-ethylthiazoline was 11 g (50%). The m.p. was 73-75°. The substance was soluble in alcohol and alkali and insoluble in water, ether, and acid.

Found %: C 40.74; H 6.04; N 9.3; S 44.03. $C_5H_9NS_2$. Calculated %: C 40.77; H 6.16; N 9.5; S 43.55.

2-Mercapto-1-aminobutane hydrochloride. A mixture of 0.8 g of 2-mercapto-5-ethylthiazoline and 20 ml of concentrated hydrochloric acid was heated in a sealed tube at 185-190° for 5 hr. After the heating, the reaction solution was evaporated to dryness in vacuum, the residue dissolved in 10 ml of anhydrous alcohol, and the alcohol solution boiled with charcoal and filtered. The addition of absolute ether to the filtrate yielded crystals. The latter were collected and washed with absolute ether. The yield of 2-mercapto-1-aminobutane hydrochloride was 0.38 g (50%). The m.p. was 134-138°.

Found %: C 33.82; H 8.38; N 9.83; S 21.77. $C_4H_{12}NSCl$. Calculated %: C 33.91; H 8.58; N 9.88; S 22.63.

SUMMARY

1. A laboratory method was developed for the preparation of β-mercaptoethylamine hydrochloride in 42% yield, calculated on the starting ethanolamine.

2. The same method was used to synthesize 1-amino-2-mercaptobutane hydrochloride, which has not been described in the literature.

3. It was shown that 5-alkyl-2-mercaptothiazolines are hydrolyzed with greater difficulty than 2-mercaptothiazoline.

4. A simple method is described for the preparation of ethyleneimine in 50.6% yield, calculated on the starting ethanolamine.

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SYNTHESIS OF ALIPHATIC TAURINES BY THE LEUCKART REACTION

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In previous work [1, 2], a description was given of the preparation of aromatic taurine homologs by reductive amination of β-keto sulfonic acids under the conditions of the Leuckart reaction. For a long time we were unable to prepare taurines from aliphatic β-keto sulfonic acids by this method. To select more suitable reaction conditions we decided to use an analytical procedure based on the following considerations.

The following processes may occur during the reaction of β-keto sulfonic acids with formamide.

1. The main reaction, namely, reductive amination.

$$R{-}CO{-}CH_2SO_3H + 2HCONH_2 \longrightarrow R{-}\underset{\displaystyle NH{-}CHO}{\underset{|}{CH}}{-}CH_2SO_3H + NH_3 + CO_2$$

The course of this reaction may be assessed from the amount of carbon dioxide liberated.

2. A side process, namely, hydrolysis of the keto sulfonic acid with the formation of a ketone; the degree of hydrolysis may be assessed from the amount of sulfate ion appearing in the reaction mixture.

3. Another side process, namely, reduction of the sulfonic acid group to hydrogen sulfide, whose smell could be detected invariably during the reaction.

Thus, if the reaction was carried out under conditions which made it possible to determine quantitatively the CO_2, $SO_4^{=}$, and H_2S, then the data obtained would provide a measure of the extent of the main and side reactions. The analytical method of studying the Leuckart reaction by the amount of CO_2 evolved has been used previously by Metayer [3] in the case of ketones.

The applicability of the analytical method was first checked on the reaction of ammonium acetophenonesulfonate with formamide as in this case it is easy to compare the analytical data with the actual yield of β-phenyltaurine, which is readily isolated quantitatively due to its insolubility in water and acids. In the experiments, ammonium acetophenonesulfonate (0.01 mole) was heated with formamide (0.04 mole) to 175° for 6-8 hr. The results of several experiments, which agreed with each other satisfactorily, indicated that the three reactions above occurred to the following extents:

1) approximately 85% of reductive amination (from the amount of CO_2 formed);
2) approximately 25% of hydrolysis (from the amount of $SO_4^{=}$ ions formed);
3) approximately 1-4% of reduction of the SO_3H group to hydrogen sulfide (which was trapped as CdS).

As not only the starting keto sulfonic acid, but also its hydrolysis product (acetophenone) naturally can undergo reductive amination, the actual yield of taurine should have approximately equaled the difference

TABLE 1

Aliphatic β-Keto Sulfonic Acids

Keto sulfonic acid	Yield (in %)	Analysis data for Ba salt		
		empirical formula	Ba content (in %)	
			found	calculated
$CH_3COCH_2SO_3H$	84.0	$C_6H_{10}O_8S_2Ba \cdot H_2O$	32.03, 31.69	31.90
$CH_3COCH(CH_3)SO_3H$	72.5	$C_8H_{14}O_8S_2Ba \cdot 2H_2O$	29.72, 29.70	29.67
$CH_3COCH(iso\text{-}C_3H_7)SO_3H$	87.2	$C_{12}H_{22}O_8S_2Ba$	27.62, 27.68	27.71
$CH_3COCH(C_6H_{11})SO_3H$	74.5	$C_{16}H_{30}O_8S_2Ba \cdot 2H_2O$	24.11, 24.25	24.11
$C_2H_5COCH(CH_3)SO_3H$	67.4	$C_{10}H_{18}O_8S_2Ba \cdot H_2O$	28.42, 28.35	28.28
$C_3H_7COCH(C_2H_5)SO_3H$	80.0	$C_{14}H_{26}O_8S_2Ba \cdot 2H_2O$	24.68, 24.49	24.56
$iso\text{-}C_3H_7COC(CH_3)_2SO_3H$	58.6	$C_{14}H_{26}O_8S_2Ba \cdot 2H_2O$	24.61, 24.81	24.56

between the amounts of CO_2 and SO_4'' formed. In actual fact the amount of β-phenyltaurine isolated in these experiments was 54-60% of theoretical.•

An analogous analytical study of the reductive amination of acetone-sulfonic acid showed that the amount of CO_2 formed was only 50-57% instead of 85% and the amount of SO_4'' ion reached 30-35%. As in this case the amount of taurine should equal the difference between the values given above, it could be expected that the reductive amination of aliphatic keto sulfonic acids could give taurines in yields of the order of 25%. At the same time, analytical experiments on the reductive amination of acetonesulfonic acid showed that a reduction in the reaction temperature (to 145° instead of 175°) produced an increase in the degree of hydrolysis and had a negative effect on the CO_2 yield.

The data obtained in analytical experiments made it possible to undertake an attempt at the preparation of aliphatic taurines. The starting materials were β-keto sulfonic acids, obtained by the action of dioxane–sulfur trioxide on ketones.

Until now there has been no conclusive demonstration of which of the two positions adjacent to the carbonyl group is occupied by the sulfonic acid group during the sulfonation of unsymmetrical ketones of the type CH_3- $-CO-CH_2-R$. To demonstrate the structure of such sulfonic acids, we synthesized both sulfonic acids of methyl ethyl ketone by the action of sodium sulfite on the appropriate bromo ketone. A mixed melting point of the sodium salt of the product from the sulfonation of methyl ethyl ketone with dioxane--sulfur trioxide with sodium 3-butanone-2-sulfonate (obtained by the action of Na_2SO_3 on methyl bromoethyl ketone [4]) was not depressed. This indicates that in this and apparently in analogous cases the sulfonation of methyl alkyl ketones involves the methylene group adjacent to the carbonyl. Data on the β-keto sulfonic acids obtained are given in Table 1.

All the β-keto sulfonic acids obtained were then subjected to the Leuckart reaction. For isolating the aliphatic taurines we were unable to use the simple method which was suitable in the case of aromatic homologs of taurine and was based on the very low solubility of aryl taurines in water and acids. Aliphatic homologs of taurine are very soluble in water and are difficult to separate by recrystallization from the inorganic salts that are formed in large amounts during the reaction. We therefore isolated the alkyltaurines as the S-benzylthiuronium salts of their N-formyl derivatives. The yields were from 16 to 42%. Data on the salts of N-formyl-α,β-alkyltaurines obtained are presented in Table 2.

EXPERIMENTAL

1. Aliphatic β-keto sulfonic acids. The starting β-keto sulfonic acids were obtained by sulfonation of ketones with dioxane–sulfur trioxide by the procedure described previously [5]. All the sulfonic acids were

• This yield is less than in preparative experiments where a formamide-formate mixture was used instead of formamide. However, we considered it advantageous to use formamide in analytical experiments so as not to have an additional volatile component (formic acid) in the mixture.

TABLE 2

Aliphatic Homologs of N-Formyltaurine

Taurine	Yield (in %)	S-Benzylthiuronium salt			
		melting point	empirical formula	N content (in %)	
				found	calculated
$CH_3CHCH_2SO_3H$ NHCHO	—	194—195°	$C_{12}H_{19}O_4N_3S_2$	12.62, 12.83	12.63
$CH_3CHCH(CH_3)SO_3H$ NHCHO	38.3	152—152.5	$C_{13}H_{21}O_4N_3S_2$	11.81, 11.93	12.09
$CH_3CHCH(iso\text{-}C_3H_7)SO_3H$ NHCHO	24.0	216—217	$C_{15}H_{25}O_4N_3S_2$	11.18, 11.35	11.19
$CH_3CHCH(C_5H_{11})SO_3H$ NHCHO	20.0	179.5—180	$C_{17}H_{29}O_4N_3S_2$	10.38, 10.53	10.41
$C_2H_5CHCH(CH_3)SO_3H$ NHCHO	16.0	178.5—179	$C_{14}H_{23}O_4N_3S_2$	11.74, 11.65	11.62
$C_3H_7CHCH(C_2H_5)SO_3H$ NHCHO	—	118—119	$C_{16}H_{27}O_4N_3S_2$	10.48, 10.70	10.78
$iso\text{-}C_3H_7CHC(CH_3)_2SO_3H$ NHCHO	42	182—183	$C_{16}H_{27}O_4N_3S_2$	11.64, 11.50	10.78

isolated as the barium salts (Table 1), which were converted into the ammonium salts by the action of an equivalent amount of ammonium sulfate for the following stages of the reaction.

Methyl ethyl ketone sulfonic acid. To 33.1 g of methyl ethyl ketone was slowly added a suspension of dioxane–sulfur trioxide in dichloroethane (obtained from 32 g of sulfur trioxide and 34 ml (35 g) of dioxane) at -4 to 0°. After standing for 12 hr, the reaction mixture was treated with a suspension of barium carbonate in water, the excess carbonate removed by filtration, and the filtrate evaporated to dryness to yield 65.2 g (72.56%) of the barium salt of methyl ethyl ketone sulfonic acid. For purification, the salt was recrystallized from water twice.

Found %: Ba 29.72, 29.76. $C_8H_{14}O_8Ba \cdot 2H_2O$. Calculated %: Ba 29.67.

Mixing equivalent amounts of aqueous solutions of the barium salt and sodium sulfate yielded the sodium salt of methyl ethyl ketone sulfonic acid, which was recrystallized twice from anhydrous alcohol. It had m.p. 141.5-144°.

3-Butanone-2-sulfonic acid. a) Bromination of methyl ethyl ketone. A mixture of 62 g of methyl ethyl ketone, 125 ml of water, and 14.7 g of potassium chlorate was stirred at 50° while 25.6 ml (80 g) of bromine was added dropwise, stirring continued for 1 hr, and the lower layer separated, shaken with magnesium oxide, washed with water, and dried with $CaCl_2$. Distillation on a column gave 31.6 g of methyl bromoethyl ketone with b.p. 86.5-88.5° at 150 mm. Literature data [6]: b.p. 86.5-88.5° at 150 mm.

b) Sodium 3-butanone-2-sulfonate. A solution of 10 g of methyl bromoethyl ketone in 50 ml of alcohol was mixed with a solution of 50 g of sodium sulfite in 50 ml of water. The solution obtained was evaporated to dryness and the residue extracted with hot anhydrous alcohol. Two recrystallizations yielded a substance with m.p. 140.5-141.5° which did not depress the melting point of the sodium salt of methyl ethyl ketone sulfonic acid, obtained by sulfonation of the ketone with dioxane–sulfur trioxide.

TABLE 3

Results of Analytical Study of the Reaction of Ammonium Keto Sulfonates with Formamide (10 mmoles of keto sulfonate + 40 mmoles of $HCONH_2$)

Starting keto sulfonic acid	Temperature	Time (in hr)	Results of analytical determinations (in millimoles)			Yield (in %)	
			CO_2	$BaSO_4$	CdO	on CO_2	on taurine
Acetophenonesulfonic acid	175°	6	8.59	2.48	0.1	85.9	54.4
	175	6	8.54	2.46	0	85.4	—
	175	6	8.75	2.64	0.2	87.5	56.9
	175	8	8.48	2.54	0.37	84.8	60.4
Acetonesulfonic acid	175	6	5.11	3.14	0.27	51.1	—
	175	6	5.6	3.5	0.23	56	—
	195	6	5.1	3.2	0.27	51	—
	145	7	3.4	4.1	0.3	34	—

Analytical study of the reductive amination of β-keto sulfonic acids. The experiments were designed so that the gaseous reaction products could be trapped quantitatively. The reaction flask was connected to a wash bottle with a weakly acid solution of cadmium sulfate for absorbing hydrogen sulfide; the precipitate of cadmium sulfide formed in it was collected by filtration, fired in air, and weighed as cadmium oxide. The wash bottle was connected to a U-tube with calcium chloride and two U-tubes with fused potassium hydroxide; the amount of carbon dioxide was determined from the increase in weight of the latter. A tube with soda lime was attached to the end of the system to prevent the entrance of moisture and carbon dioxide from the air. A gentle stream of dry nitrogen was passed through the whole system during the reaction. For the determination of sulfate ion, at the end of the experiment the contents of the reaction flask were dissolved in water, barium chloride solution added, and the barium sulfate precipitate collected by filtration, fired, and weighed. The filtrate was acidified with hydrochloric acid and boiled for 30 min; in experiments with acetophenonesulfonic acid, this precipitated the difficultly soluble β-phenyltaurine. The starting materials, namely, the ammonium keto sulfonate and formamide, were used in molar ratios of 1 : 4. The results are given in Table 3.

Alkyltaurines. N-Formyl-β-methyltaurine. A mixture of 11 g of ammonium carbonate and 23 ml of 85% formic acid was heated to 185° in a Wurtz flask attached to a distillation condenser. When the mixture had cooled to 60-70°, 15.5 g of ammonium acetonesulfonate was added. The reaction mixture was heated to 180° for 6 hr, dissolved in 60 ml of water, and the solution obtained treated with a solution of 9 g of S-benzylthiuronium chloride in 30 ml of water. The crystalline precipitate, which formed as the solution stood, was collected and recrystallized from 50% alcohol. It had m.p. 194-195°.

Found %: C 43.08, 43.27; H 5.47, 5.56; N 12.62, 12.83. $C_{12}H_{19}O_4N_3S_2$. Calculated %: C 43.24; H 5.70; N 12.63.

The same procedure was used for the synthesis of the remaining homologs of N-formyltaurine given in Table 2.

SUMMARY

1. The action of dioxane–sulfur trioxide on aliphatic ketones yielded aliphatic β-keto sulfonic acids, which were subjected to reductive amination by the Leuckart reaction and thus converted into taurine homologs that were isolated as the S-benzylthiuronium salts of their N-formyl derivatives.

2. The course of the reductive amination of β-keto sulfonic acids was studied by means of an analytical procedure.

3. It was shown that the sulfonic acid group enters the methylene unit during the sulfonation of ketones with the structure $CH_3–CO–CH_2–R$.

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LIPIDS

IV. STUDY OF UNSATURATED GLYCERIDES BY PAPER CHROMATOGRAPHY

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Up to the present time the glyceride composition of most fats and oils has been studied inadequately as available physicochemical analysis methods do not guarantee an accurate demonstration of the structure of position isomers of natural glycerides [1]. The relative position of acid residues in individual compounds may be determined only by comparing them with synthetic samples of strictly established structure. One such method for investigating glycerides is paper chromatography, which may be used successfully, for example, for the separation of polycomponent acid mixtures obtained during the hydrolysis of fats [2, 3]. Available communications on the chromatography of glyceride mixtures do not yet give sufficient experimental data for drawing conclusions on the efficiency of this method in the lipid series [4].

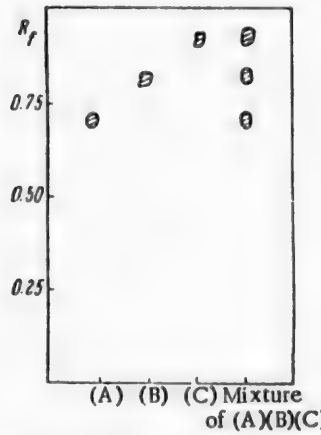

Fig. 1. R_f values for monoglycerides. A) α-Oleyoylglycerol; B) α-linoleoylglycerol; C) α-linolenoylglycerol.

The present article gives a description of an investigation of synthetic unsaturated glycerides by means of inverse-phase chromatography on paper.

The subjects for investigation were the monoglycerides α-oleoylglycerol (A), α-linoleoylglycerol (B), and α-linolenoylglycerol (C), and also the triglycerides α,α'-dilinoleoyl-β-stearin, LSL (I), α-stearoyl-β, α'-dilinolein, SLL (II), α-linoleoyl-β, α'-diolein, LOO (III), α-stearoyl-β-linolenoyl-α'-olein, SLnO (IV), α,α'-dilinoleoyl-β-olein, LOL (V), trilinolein, LLL (VI), α-stearoyl-β,α'-dilinolenoin, SLnLn (VII), α,α'-dilinolenoyl-β-stearin, LnSLn (VIII); α,α'-dilinoleoyl-β-linolenin, LLnL (IX), α-linolenoyl-β,α'-dilinolein, LnLL (X), α-linoleoyl-β,α'-dilinolenin, LLnLn (XI), and trilinolenin, LnLnLn (XII). We described the synthesis of all these compounds in previous communications [5].

EXPERIMENTAL

The experiments with the α-monoglycerides (A), (B), and (C) were carried out on paper from the Volodarskii Factory, Leningrad (1957 issue) by the procedure for aliphatic acids [6] with the system silicone (Type 2) [acetic acid–water mixture (75 : 25)]. The following R_f values were obtained: 0.70, 0.81, and 0.91 (Fig. 1).

In the work with triglycerides, the paper was first dried at 120° for 2 hr and then impregnated with a 5% ether solution of silicone (Type 2). The stationary phase was a fraction of kerosene alkanes with b.p. 150-200° at 758 mm and the mobile phase was a mixture of acetone and water (95 : 5), saturated with this hydrocarbon fraction.

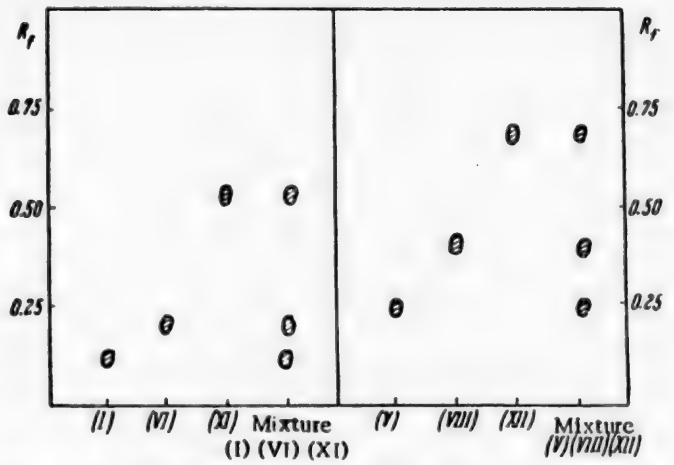

Fig. 2. R_f values of triglycerides. (I) – LSL, (V) – LOL, (VI) – LLL, (VIII) – LnSLn, (XI) – LLnLn, (XII) – LnLnLn.

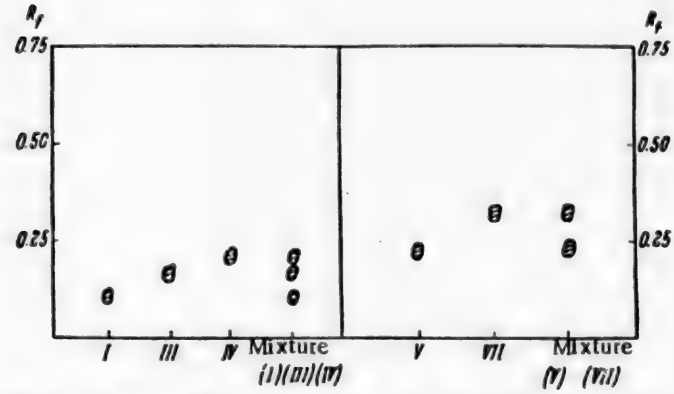

Fig. 3. R_f values of triglycerides. (I) – LSL, (III) – LOO, (IV) – – SLnO, (V) – LOL, (VII) – SLnLn.

R_f Values of Triglycerides

Triglyceride	No. of double bonds	R_f
LSL (I)	4	0.10
SLL (II)	4	0.12
LOO (III)	4	0.16
SLnO (IV)	4	0.20
LOL (V)	5	0.24
LLL (VI)	6	0.26
SLnLn (VII)	6	0.32
LnSLn (VIII)	6	0.40
LLnL (IX)	7	0.47
LnLL (X)	7	0.49
LLnLn (XI)	8	0.53
LnLnLn (XII)	9	0.68

With a micropipette we placed 50-γ samples of the substance in the form of a 1% ether solution at equal distances from each other and 5 cm from the lower edge of a sheet of paper (6 × 20 cm) soaked in a 10% solution of the hydrocarbons in acetone. The paper was placed in a hermetically sealed, 1-liter cylinder (7 cm in diameter and 30 cm high), containing 60 ml of the mobile phase. The substances were irrigated for 4-6 hr and then the chromatogram was dried at 110-120° and treated with a 0.1% aqueous alcohol solution of Sudan black, which gives characteristic dark blue spots on a gray-blue background with triglycerides. The indicator was sensitive to 10-12 γ. The R_f values obtained are given in the table.

The triglycerides LSL (I), LLL (VI), and LLnLn (XI) and also LOL (V), LnSLn (VIII), and LnLnLn (XII), which differ in the degree of unsaturation, have very different R_f values so that mixtures of them are separated very readily (see Fig. 2).

In the case of compounds with the same number of double bonds but with different acid residues, namely LSL (I), LOO (III), and SLnO (IV) and LLL (VI) and SLnLn (VII) the R_f values are closer though the separation of such mixtures is also possible (Fig. 3).

This method is less effective for the separation of the position isomers LSL (I) and LLS (II), LnSLn (VIII) and SLnLn (VII), LLnL (IX) and LnLL (X), but it still makes it possible to determine them.

SUMMARY

1. Synthetic α-mono- and triglycerides were studied by means of inverse-phase paper chromatography.

2. It was shown that this method may be used for separation and identification of both unsaturated monoglycerides and mixtures of triglycerides differing in the degree of unsaturation and also mixtures of triglycerides with the same number of double bonds, but with different acid substituents.

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REDUCTION OF MYRCENE MONOXIDE WITH LITHIUM ALUMINUM HYDRIDE

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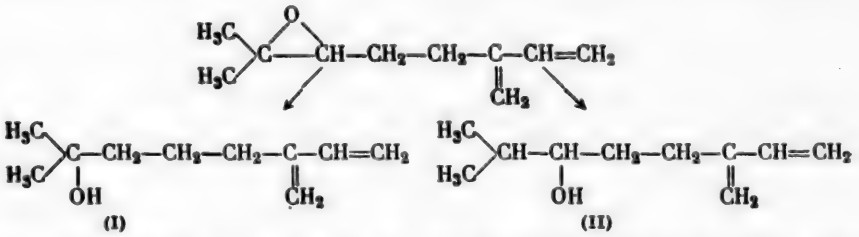
According to investigations in our laboratory, the catalytic hydrogenation of terpene oxides does not always give the desired results. In some cases (linalool and myrcene oxides) [1] the absorption of hydrogen is not complete and in others (menthene oxides) [2], the reaction is complicated by side processes.

Lithium aluminum hydride was found to be a more convenient reducing agent, leading to the formation of the corresponding alcohols from the oxides. Thus, Mousseron and his co-workers [3] obtained the tertiary alcohol 1-methylcyclohexanol-1 by reduction of 1-methylcyclohexene-1 oxide. Reduction of limonene monoxide with lithium aluminum hydride formed a mixture of the tertiary and secondary alcohols β-terpineol and D-neodihydrocarveol [4].•

In the present investigation we studied the reduction of myrcene monoxide with lithium aluminum hydride. As a result of the reduction, we isolated two alcohols with the composition $C_{10}H_{18}O$ with different properties (see the table).

The reduction of myrcene monoxide apparently proceeded in two directions to form the tertiary alcohol 2-methyl-6-methyleneocten-7-ol-2 (I) and the secondary alcohol 2-methyl-6-methyleneocten-7-ol-3 (II).



(I) (II)

The alcohol with b.p. 50-52° (1.5 mm) and the lower specific gravity was assigned the structure of the tertiary alcohol (I). The other alcohol with the higher boiling point and the greater specific gravity was apparently the secondary alcohol (II). The presence of conjugated double bonds in the molecules of the alcohols obtained followed from an analysis of their infrared spectra. The spectra of both alcohols contained bands characteristic of conjugated double bonds: in the spectrum of the supposed tertiary alcohol (I) at 1596 and 1635 cm^{-1} and in the spectrum of the secondary alcohol (II) at 1593 and 1642 cm^{-1}.

In addition, both spectra contained bands of CH deformation vibrations in the groups $-CH = CH_2$ and $> C = CH_2$ at 993, 903, and 897 cm^{-1} in the spectrum of alcohol (I) and 993, 908, and 898 cm^{-1} in the spectrum of alcohol (II).

•The recent investigations of Kuczinski and Piatkowski [5] showed that in the given case β-terpineol is present in the form of two stereoisomers: trans-β-terpineol and cis-β-terpineol.

Properties of Alcohols Obtained by Reduction of Myrcene Monoxide with Lithium Aluminum Hydride

Boiling point (pressure in mm)	d^{20}_4	$n^{20}D$
50-52° (1.5)	0.8760	1.4646
61-63 (1.0)	0.8765	1.4698

The bands at 1126 and 1203 cm^{-1}, which were present in both spectra, can be ascribed with a certain degree of probability to the presence of secondary and tertiary alcohol groups. The presence of these two bands in both spectra indicates that the two alcohols obtained were not separated completely by fractionation.

We should also mention that the alcohols we isolated had a great tendency to polymerize; samples of these alcohols polymerized completely after several months in sealed ampoules.

EXPERIMENTAL

Preparation of myrcene. Myrcene was preparated by dehydration of linalool (α_D + 12.1°, d^{20}_4 0.8651, $n^{20}D$ 1.4627), isolated from coriander oil. The dehydration was carried out in the presence of iodine at 102-110° (150-160 mm).

B.p. 58-59° (12 mm), d^{20}_4 0.7961, $n^{20}D$ 1.4719, MR_D 47.82; calc. 46.97.

Preparation of myrcene monoxide. Myrcene monoxide was obtained by oxidation of myrcene with acetyl hydroperoxide.

B.p. 68-69.5° (10 mm), d^{20}_4 0.8701, $n^{20}D$ 1.4626, MR_D 48.03; calc. 46.89.

Reduction of myrcene monoxide with lithium aluminum hydride. A solution of 25.5 g of myrcene monoxide in 200 ml of dry ether was placed in a three-necked flask with a stirrer with a mercury seal, a dropping funnel, and a reflux condenser with a calcium chloride tube. A stream of dry nitrogen, freed from impurities, was then passed for 15-20 min and 118 ml of an ether solution of lithium aluminum hydride containing 6.3 g of $LiAlH_4$ slowly added dropwise. The addition rate was such that there was a slow flow of condensed ether from the reflux condenser. When all the solution had been added, stirring was continued for 3-4 hr. The excess lithium aluminum hydride and the complex formed were decomposed with water (with external cooling of the reaction mixture with ice and water). Water was carefully added dropwise until the ether no longer boiled. Then a further 200-300 ml of water was added and the clear liquid decanted from the residue. The ether layer was separated from the aqueous layer and washed with water until neutral. The residue remaining in the reaction flask was treated with concentrated (40%) alkali and extracted three times with ether and the ether extracts added to the main ether solution. The solution was dried and the ether removed by distillation. The residue was vacuum distilled (3 mm) over the temperature range 55-70°. The yield was 20.5 g and the residue (polymer) weighed 3 g. The reduction experiment was repeated.

The mixture of products (30 g) obtained by reduction of myrcene monoxide was fractionated repeatedly. Two fractions were isolated as a result: the 1st fraction had b.p. 50-52° (1.5 mm) and weighed 5.5 g (tertiary alcohol) and the 2nd fraction had b.p. 61-63° (1.0 mm) and weighed 7.9 g (secondary alcohol).

1st fraction, b.p. 50-52° at 1.5 mm.

Found %: C 77.83, 77.91; H 11.88, 11.92. Number of OH groups 1.03, 1.02. M 154.1, 158.2. $C_{10}H_{18}O$. Calculated %: C 77.86; H 11.76. Number of OH groups 1.0. M 154.24.

Infrared absorption spectrum • ν: 1635 (w), 1596 (s), 1459 (s), 1383 (vs), 1203 (s), 1150 (s), 1126 (s), 1060 (w), 993 (s), 943 (w), 903 (shoulder) 897 (vs).

2nd fraction, b.p. 61-63° at 1.0 mm.

Found %: C 77.74, 77.80; H 11.77, 11.66. Number of OH groups 1.08, 1.06. M 153.7, 154.9. $C_{10}H_{18}O$. Calculated %: C 77.86; H 11.76. Number of OH groups 1.0. M 154.24.

Infrared absorption spectrum ν: 1642 (w), 1593 (s), 1464 (s), 1370 (vs), 1205 (s), 1150 (s), 1126 (s), 1042 (w), 993 (s), 941 (w), 908 (shoulder), 898 (vs).

• The infrared absorption spectra were obtained with an IKS-11 spectrometer. The layer thickness was 10 μ. The approximate intensities of the absorption bands are denoted by the following: w—weak, s—strong, vs—very strong.

SUMMARY

The reduction of myrcene monoxide with lithium aluminum hydride led to the formation of two alcohols with the composition $C_{10}H_{18}O$. One of these was apparently tertiary and the other secondary.

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HEATS OF SOLUTION OF THE HEXAHYDRATES OF COBALT AND NICKEL PERCHLORATES

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In continuing a systematic investigation of the crystal hydrates of perchlorates, we measured the heats of solution in water of the hexahydrates of cobalt and nickel perchlorates. We presented the experimental procedure previously [1, 2].

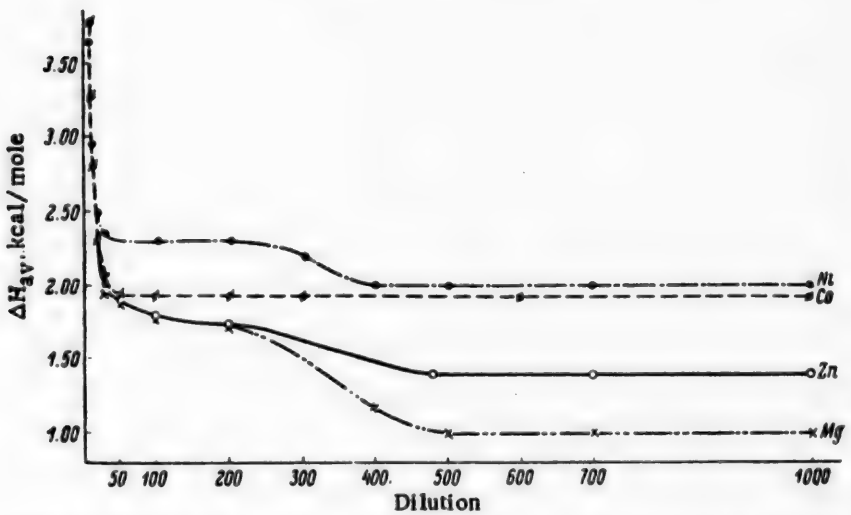
For determining the heats of solution we used the hexahydrates, which contain 6.00 molecules of water per mole of anhydrous salt. The composition of the preparations was checked by parallel analysis of the hexahydrate for Co^{2+} and Ni^{2+} ions and also for ClO_4^- ion. The Co^{2+} and Ni^{2+} were determined by titration with Trilon B with murexide as indicator and the ClO_4^- ion by reduction of ClO_4^- to Cl^- with subsequent analysis for Cl^- ion by Mohr's method. The accuracy of the analyses for Co^{2+}, Ni^{2+}, and ClO_4^- ions was ~ 0.02-0.03%. The preparation was only used for determination of the heats of solution if the analysis data for the anion and cation agreed with the theoretical values. Thus, for example, in the analysis of one preparation we obtained Co 17.09% (theoretical 17.10) and Cl 19.39% (theoretical 19.38). Average data obtained from 5-7 experiments at 25° are given in the table and the figure.

As the data presented show, the heats of solution of nickel perchlorate hexahydrate for dilutions of 1 : 1000, 1 : 700, 1 : 500, and 1 : 400 were practically identical. Consequently, the dilution of 1 : 400 is the limit. The value of the thermal effect, which equals 2.00 kcal/mole, may be taken as the first integral heat of solution. With a further increase in the solution concentration, the endothermal effect of the solution of nickel perchlorate hexahydrate does not increase monotonically. Over the dilution range from 1 : 200 to 1 : 30, the heat of solution of $Ni(ClO_4)_2 \cdot 6H_2O$ hardly changes and there is a second plateau on the curve of the relation between the heat of solution and the salt concentration. In contrast to the behavior of the nickel salt, during solution of cobalt perchlorate hexahydrate the heat of solution was practically the same for all dilutions over the concentration range from 1 : 1000 to 1 : 30. The heats of solution of hexahydrates of zinc and magnesium perchlorates, which we published previously, are also plotted on the figure for comparison. For all four hexahydrates, at a dilution of approximately 1 : 30 there was a clearly expressed bend on the curve, which appeared to divide the whole curve into two portions belonging to concentrated and dilute solutions. The figure also shows that beginning with a dilution of 1 : 30, the heats of solution of all four hexahydrates in concentrated solutions were identical within the limits of experimental error.

With the formation of dilute solutions, the heats of solution of Mg, Zn, Co, and Ni perchlorate hexahydrates differed. In limiting dilute solutions there is complete hydration of the ions and, consequently, the chemical individuality of the corresponding free ions should appear most fully. As the figure shows, the least endo effect and consequently the strongest interaction of the cation with water occurs during the solution of magnesium perchlorate hexahydrate and this interaction decreases in the series Mg > Zn > Co > Ni.

The acidity of the corresponding solutions may also serve as a measure of the interaction of the cation with the solvent. The stronger the M-OH bond in the aquo salt formed, the higher will be the acidity of the solution.

Dilution	ΔH_{av}, kcal/mole	
	$Ni(ClO_4)_2 \cdot 6H_2O$	$Co(ClO_4)_2 \cdot 6H_2O$
1 : 100	2.00 ± 0.04	1.93 ± 0.03
1 : 700	2.00 ± 0.04	1.93 ± 0.03
1 : 500	2.00 ± 0.04	—
1 : 400	2.00 ± 0.04	—
1 : 300	2.20 ± 0.04	1.93 ± 0.03
1 : 200	2.30 ± 0.04	1.93 ± 0.03
1 : 100	2.30 ± 0.04	1.93 ± 0.03
1 : 50	2.30 ± 0.04	1.93 ± 0.03
1 : 30	2.34 ± 0.04	2.04 ± 0.93
1 : 20	2.49 ± 0.04	2.29 ± 0.93
1 : 13	2.95 ± 0.04	2.82 ± 0.93
1 : 10	3.30 ± 0.04	3.29 ± 0.93
1 : 8.75	3.64 ± 0.04	—
1 : 7.6	—	3.80 ± 0.93



Heats of solution of hexahydrates of Ni, Co, Zn, and Mg perchlorates at various dilutions.

According to data in [3, 4], perchlorates may be arranged in the following series with respect to decreasing acidity: Zn > Co > Ni. Thus, for Zn, Co, and Ni perchlorates there is correspondence between the changes in the heats of solution and the acidity of the solution.

As regards average dilutions (from 1 : 300 to 1 : 30), this region may be regarded as transitional between concentrated solutions and the limiting dilution.

SUMMARY

1. The heats of solution of the hexahydrates of nickel and cobalt perchlorates were investigated over a wide range of dilutions.

2. It was shown that with the formation of concentrated solutions, the heats of solution of the hexahydrates of Mg, Zn, Co, and Ni perchlorates are practically identical.

3. With the formation of limiting dilute solutions, the endo effect of solution increases in the following series : Mg < Zn < Co < Ni.

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LETTERS TO THE EDITOR

PREPARATION OF ORGANOTIN COMPOUNDS WITH A VINYLACETYLENE RADICAL

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The condensation of vinylacetylides with various primary halogen derivatives yielded a series of homologs of vinylacetylene [1, 2]. The reaction of vinylacetylenylmagnesium bromide with various alkylchlorosilanes yielded silicon-containing vinylacetylenes [3].

We were able to show that this method readily yields vinylacetylenes containing other Group IV elements. Thus, the action of trimethyl- and triethyltin chloride on vinylacetylenylmagnesium bromide yielded trimethylbuten-3-yn-1-yl-and triethylbuten-3-yn-1-yltin. Both liquids are colorless liquids with a mustard smell. They are readily hydrolyzed in air. When brominated in chloroform, they are cleaved at the C-Sn bond, apparently with the formation of bromovinylacetylene.

In the infrared spectra the multiple bond groupings are characterized by the frequencies: 3102 (ν_{CH}), 2130 ($\nu_{C\equiv C}$), 1592 ($\nu_{C=C}$), 960 (δ_{CH}) and 920 (δ_{CH}) cm^{-1}.

Trimethylbuten-3-yn-1-yltin.

B.p. 46.5-47° (10 mm). d^{20}_4 1.3066, $n^{20}D$ 1.5067.

Found %: C 39.13, 39.43; H 5.89, 5.84; Sn 55.00, 54.63. $C_7H_{12}Sn$. Calculated %: C 39.13; H 5.63; Sn 55.24.

Triethylbuten-3-yn-1-yltin

B.p. 89.5-90.0° (10 mm), d^{20}_4 1.2181, $n^{20}D$ 1.5098.

Found %: C 46.58, 46.49; H 7.06, 7.37; Sn 46.35, 46.46. $C_{10}H_{18}Sn$. Calculated %: C 46.74; H 7.06; Sn 46.20.

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ADDITION OF LITHIUM PHOSPHIDES TO VINYLACETYLENES

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It was previously shown that lithium dialkylamides add readily to vinylacetylenes to form allene or acetylene amines [1]. In continuing the study of the reaction of lithium heteroorganic compounds with unsaturated hydrocarbons, we established that lithium dialkylphosphides also add to vinylacetylenes in the cold. Thus, for example, when an ether solution of the reaction product of lithium diethylphosphide and vinylethylacetylene was treated with water we obtained 1-diethylphosphinohexadiene-2,3.

B.p. 78-79° (5 mm). d^{20}_4 0.8569, $n^{20}D$ 1.5025.

Found %: C 70.74; H 11.23; P 18.10. $C_{10}H_{19}P$. Calculated %: C 70.55; H 11.25; P 18.20.

The structure of the phosphine obtained was determined from the infrared spectrum. Intense bands of an allene grouping (1958 and 876 cm^{-1}) were found. Double and triple bond frequencies were absent from the spectrum.

The substance had the characteristic smell of phosphines. It fumed in air and rapidly resinified (all work with the substance was carried out in an argon atmosphere).

The reaction described is a new method of preparing unsaturated alkylphosphines from unsaturated hydrocarbons.

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EMPIRICAL FORMULA OF ABIENOL

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In 1942 Winhaus and Mucke [1] isolated from the resin of Abies pectinata D.C. the tertiary alcohol abienol in the form of the crystal hydrate with m.p. 62° and $[\alpha]_D$ + 18.8°. These authors assigned the empirical formulas $C_{17}H_{30}O_2$ and $C_{17}H_{28}O$ to abienol hydrate and abienol, respectively.

In studying the products of the secretory activity of Siberian fir (Abies sibirica Ldb.), we detected abienol [2, 3], which was isolated in the form of abienol hydrate (m.p. 63-65°, $[\alpha]_D$ + 19.5°). A more careful investigation of abienol hydrate and its derivatives compelled us to reject the formula proposed by Winhaus and Mucke. As our analyses show• (see the table), the formulas $C_{20}H_{36}O_2$ and $C_{20}H_{34}O$ are more acceptable for abienol hydrate and abienol.

Elementary Analysis Data for Abienol and Its Derivatives (in %)

Compound	Found		Empirical formula	Calculated	
	C	H		C	H
Abienol hydrate	77.54	11.81	$C_{20}H_{36}O_2$	77.86	11.76
	77.70	11.80			
	78.22	11.83	$C_{17}H_{30}O_2$	76.62	11.37
	78.16	11.88			
Abienol	82.45	11.86	$C_{20}H_{34}O$	82.69	11.80
	82.58	11.83	$C_{17}H_{28}O$	82.25	11.37
Abienol polymer	82.53	11.78	$(C_{20}H_{34}O)_n$	82.69	11.80
	82.44	11.76	$(C_{17}H_{28}O)_n$	82.25	11.37
Dihydroabienol (m.p. 92-94°)	81.98	12.38	$C_{20}H_{36}O$	82.13	12.40
	81.73	12.34	$C_{17}H_{30}O$	81.60	12.08

In accordance with this, the polymer of abienol [3], and dihydroabienol have the formulas $(C_{20}H_{34}O)_n$ and $C_{20}H_{36}O$. It should also be noted that determination of the molecular weight of dihydroabienol gave the value 305, corresponding to the formula $C_{20}H_{36}O$ (calculated M 292).

All that has been presented above indicates that abienol is a diterpene bicylic alcohol.

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•The analyses were carried out by the method of Körble [4] with silver permanganate.

[2] G. V. Pigulevskii and V. G. Kostenko, Vestn. LGU, No. 4, Ser. Fiz. Khim. 154 (1959).

[3] G. V. Pigulevskii and V. G. Kostenko, Doklady Akad. Nauk SSSR 128, 305 (1959).•

[4] Körble, Chem. Listy 49, 862 (1955).

•Original Russian pagination. See C. B. translation.

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.– Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.